D I P H T H E R I A (with cases).

A THESIS PRESENTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

IN

EDINBURGH UNIVERSITY.

APRIL 1907.

BY

P A T R I C K K I N M O N T,

M.B.: B.Ch.: F.R.C.S.E.

CONTENTS.

D I P H T H E R I A.

(French, Diphthérite - German, Diphtherie - Greek, διφθέρα a skin.)

HISTORY.

DIPHTHERIA is one of the oldest epidemics affecting the human race; the name LE DIPHTHERITE or DIPHTHERITIS was given to the disease by Bretonneau, who described to the French Académie de Médecine epidemics which occurred at Tours in the early part of the 18th Century. The disease can be traced under various names back almost to the Homeric period of Grecian History. It was known and described by Aretaeus of Cappadocia, a Greek Physician, as early as the 2nd Century A.D. and again in the 5th Century by Aetius, also a Greek Physician. Aretaeus believed the disease originated in Egypt and Syria, and hence the name "Malum Aegyptiacum", "Egyptian or Syrian Ulceration" applied by him to the disease: Aretaeus refers in his description of the malady to the Tonsils being covered with "Quodam concreto humore albo", a thick moist material which spreads to other parts of the mouth.

Aetius, in describing a pestilential throat inflammation in the 5th Century, refers to paralysis of deglutition as a result of the attack: Again, in 1557, the malady was described as an epidemic in Holland by Forest.

During the early part of the present Century, Diphtheria, or as it was then called, Croup, occurred mainly in sporadic form, and between 1855 and 1858 became epidemic in Great Britain and many other parts of the world: It extended through Spain where it went under the name of "Garotillo" when it attacked the Larynx, Fregar where it was confined to the mouth. In Italy it was described by Carnevali, Scambetti, Ghisi and others: In France by Chomel (Diss. sur le mal gorge gangreneux 1749) : In Germany by Scobinger (Diss. de morbo strangulatorio seu maligno fancium carbunculo 1650) : In England by Fothergill Huxam and others. In America, Danforth lost 4 out of his eleven children within a fortnight by a "malady of the bladders in the windpipe".

These general descriptions were probably not exact, as the observers did not always avoid confounding the disease with Scarlatina and other affections.

The earliest records of epidemic throat diseases referred to in this country are by Noah Webster in his "History of Epidemic and Pestilential Diseases"(published in 1800). Recalling the fact that "in 1389 appeared a singular meteor in the Heavens" he adds that "the year was remarkable for the death of children in all parts of England", the cause being "a species of Angina". This author gives a description of the epidemic which is extremely interesting because it seems to bring out the

main features of the disease as we know it at the present time. Webster describes the scourge as "attacking the young in sequestered situations, in Country places rather than in populous Cities", and adds that "its virulence seemed to be greatly augmented by cold and wet weather; also that its principal ravages were amongst persons under the age of puberty". Again he tells us "it was not always attended by great prostration of strength, for many persons were often walking about an hour or two before their death."

The paper by Bretonneau, of Tours, above referred to, was published in 1826, and contains the earliest accurate clinical observations on Diphtheria. He proposed the term "Diphtheritis" because of its essential characteristic namely, the formation of false membrane. Subsequently the name "Diphtheria" was proposed by Trousseau.

Bretonneau regarded the exudate as an essential part of the disease, and constituting the only source of infection, and believed that the contagion spread, not through the atmosphere, but by inoculation resulting from particles of the exudate in fluid or dust-like state coming into contact with a moist mucous membrane. He further concluded that Croup and Diphtheria were identical affections, the difference being that in Croup the diseased process extended into the Larynx and Trachea. At first he regarded Diphtheria as a wholly local disease, but later admitted that systematic poisoning was an essential pathological

condition. Since the publication of this paper by Bretonneau abundant literature has appeared by French, German and English writers which expressed some conflicting opinions regarding the nature of the disease. Some regarded the exudate as a local expression of a constitutional disease showing itself by preference on mucous membrane just as a rash of Scarlet Fever does upon the skin. This view was opposed by the ablest writers, and in the light of our present day knowledge must be regarded as untenable. The greatest difference of opinion was perhaps whether Diphtheria and membranous Croup were identical diseases or distinct morbid processes. Bretonneau held they were identical, contending that no clinical or pathological difference existed between them, but Virchow and others believed otherwise. While this question cannot yet definitely be considered as settled I believe that, at the present day the leading authorities, clinical and pathological, admit their specific identity.

The relation which exists between micro-organisms and diphtheria dates back over a century or more. In 1868 Oertel discovered bacteria in the false membrane, and these were also demonstrated by Eberth and others, but to Klebs of Zurich, belongs the honour of discovering the true bacillus of diphtheria, about the year 1883. Klebs never definitely announced that he was able to obtain true cul - tures of it, and so it must be admitted he failed to establish the causal relationship to the disease. This

relationship was established in 1884 by Loeffler (Mittheil Ans dein Kaiser Gesundheitsamte, 1884, Bd XI) who succeeded in obtaining pure cultures of the organism, also in proving its specific character by communicating diphtheria to animals by inoculating them with the organism. This discovery finally settled the dispute as to whether diphtheria is primarily a constitutional or a local disease in favour of the latter, and has moreover placed the study of diphtheria on a scientific basis.

Roux and Yersin (Ann. de l'Institut.Pasteur 1888-1889) studied the effects of the diphtheria toxin elaborated by the bacilli, an investigation which led up to the development of Serum Therapy.

DEFINITION.

DIPHTHERIA is an acute inflammatory infectious disease generally of mucous membranes, due to the invasion of a specific micro-organism, the bacillus diphtheriae of Klebs-Loeffler, characterised by the production in most cases of a false membrane at the seat of the infection and leading in many cases to a peculiar form of paralysis due to the absorption of toxic products generated by the bacillus.

From the derivation of the word it would appear as though the disease Diphtheria was dangerous mainly from a mechanical or obstructive point of view-but while this is, of course, important in cases affecting the Larynx and Trachea, the chief danger in the majority of cases arises from the Toxaemia resulting from absorption of the Toxines.

CHAPTER 11.

ETIOLOGY.

Diphtheria is epidemic at the present day in widely spread areas. Like all other contagious diseases Diphtheria occurs sometimes sporadically, endemically and at others epidemically. In explaining these circumstances consideration must be given not only to the "causa causans", or specific germ, but also to the "causa efficiens", or that which determines the occurrence of widespread epidemics, such as sanitary surroundings, climate, sex, rainfall, season and environment, all of which affect the individual receptivity to the infection. It is worth of note that before the year 1880 the Urban incidence was relatively smaller than Rural incidence, whereas in the last twenty years, though both have increased, the urban incidence has been relatively the larger. Possibly improved means of transit may to a certain extent account for this. (Newsholme Origin and Spread of Pandemic Diphtheria, p.138)

Diphtheria has a marked seasonal prevalence, this being largest during October, November and December, and least of all in July.

There is much diversity of opinion as to the exact controlling influence of Soil and Climate. Amongst

older writers it was a common impression that low, damp, marshy soil where drainage was bad and where there was much decaying vegetable matter favoured the developement of the malady, while on the other hand, a hard dry soil, or a soil composed largely of dry sand has been regarded as unfavourable to the spread of the disease.

Lennox Browne (Diphtheria & its assoc.) bears out the opinion of Thorne Thorne (Nat. Hist. of Diphtheria) that a clayey soil is suitable for the spread of epidemics, the retentive nature as regards moisture and organic refuse are influences tending to the fostering and fatality of Diphtheria.

Thorne adds that "Clays of such configuration as admit of natural drainage are not unlikely to be associated with comparative immunity from Diphtheria in one district, whereas sands and gravels which fill up basins in underlying impervious strata and thus become engorged with water may have a share in producing an opposite result." (loc.cit.p28.)

Thorne is careful to explain, however, that he does not wish to attach too much importance to the influence of site, soil, and climate apart from other considerations which come into play and exert an influence on the course of epidemics.

Hirsch, on the other hand, makes statements which are quite the reverse of Thorne's ; he asserts that the disease has been found to be much less prevalent in valleys than at higher elevations, and in dry rather than in damp situations, and that in England the sickness was met with under no special conditions of locality, but occured equally on sand and loam and on high ground as well as on low. (Thorne Nat.Hist.Diphtheria) p 18)

The researches of Newsholme (Origin & spread of Pandemic Diphtheria 1898) are probably the most reliable on this question, his conclusions being so important as to warrant production of a summary thereof:--

1. An Epidemic of Diphtheria never originates where there has been a series of years in which each year's rainfall is above the average amount.

2. An epidemic never originates or continues in a wet year unless this wet year follows on two or more dry years immediately preceding it.

3. Those epidemics for which accurate statistics are available have all originated in years when the total rainfall is below the average: the greatest epidemics have occurred when there have been four or five consecutive dry years.

It will be noticed that those conclusions are at

variance with the older idea that Diphtheria was more prevalent in wet and damp seasons and soil.

AGE plays an important role in the Incidence and Mortality of Diphtheria which shews marked predilection for children. The London notifications from 1892-1897 shew that about one-third of the cases occur before the age of five years and rather less than one-third between five and ten years. Each succeeding Quinquennium shows a smaller number of notifications (Encyclopoedia Medica Vo. 3.p.3.)

The case mortality likewise is highest in the first five years of life and especially in infants under a year.

The reports of the Metropolitan Asylums Board, before Antitoxin treatment was introduced show that the mortality

Under 5 years of age	=	50%
Between 5 & 10	=	10%
" 15 & 20	=	4%
" 20 & 40	=	5%
Over 40	=	17%

SEX. Diphtheria appears to be more common in females than in males. Between the ages of 5 and 10 years girls are one-third more liable than boys. Kissing among girls more than boys probably accounts for this.

NATURE OF THE INFECTION AND SPREAD OF DIPHTHERIA.

The contagion as a rule is transmitted from one person to another through the medium of the pharyngeal buccal and nasal secretions. The dust of a sick room or school contaminated with particles of dried secretions may serve to carry the infection for a short distance by the medium of the atmosphere. Where disinfection has received no attention it is disseminated by means of infected articles such as clothing, books, towels, toys and such like articles. Among poor children the habit of passing sweets from mouth to mouth affords a ready means of transmission of the disease from one child to another. The bacillus, however, when due care is taken does not seem readily transmitted through the air to other cases, those nursing being most likely to become infected. Thorne is of opinion that the diphtheria contagion in regard to aerial transmission resembles Typhus more than Small Pox in that it is little likely to produce disease after being subjected to conditions such as are involved in transmission by wind currents. During my residency at Dundee Royal Infirmary it was the custom to admit urgent cases of Diphtheria for Tracheotomy into the general children's Ward, the plan adopted being to surround the cot with a tent freely impregnated with some disinfectant. In this

Hospital there never has been a case where another child in the Ward became infected with Diphtheria, and during my 18 months residence there was not a single Nurse who contracted infection. The Medical Superintendent, moreover, informs me that in his experience he only knew of one case where a Nurse was doubtfully infected, the diagnosis being uncertain and no paralytic phenomena ensuing; Where other means are available this plan of mixing cases cannot be recommended: During my residency at Lincoln County Hospital where at one time a case of Diphtheria occurred in the children's ward several Nurses promptly developed the disease. Possibly at Dundee where the Nurses knew they were dealing with severe cases more stringent precautions were taken as regards their own throats by frequent use of gargles etc.

Pasteur (Gibson's Medicine, Vol.1.p.199) records a case where outbreaks occurred at intervals in a hospital ward in face of most stringent precautions until the old flooring was taken up and replaced by a new one. In his case the germs probably lurked in the chinks between the boards and were dislodged by cleansing and sweeping operations.

In epidemics occurring at intervals in hospital wards, without obvious cause, search should be made into the throats of the nursing staff for possible means of infect-

ion. An epidemic broke out at Hull Royal Infirmary in the Children's Ward and was traced to this source; one Nurse actually shewed membrane in her throat, and yet had not complained of "sore throat". Swabs were taken from 9 Nurses who had been in contact with the children, and the Klebs-Loeffler bacillus was obtained in six out of the 9. After free spraying with chlorine the epidemic ceased. (Brit. Med. Jour. May 21, 1904.)

THE INFLUENCE OF SCHOOL LIFE on the spread of Diphtheria has been the subject of important researches. The bringing together of children who by their age are most susceptible to infection, the close association of such children in a vitiated atmosphere for many hours in a day - the faulty sanitary conditions of some Schools tending to favour sore throats and impaired general health, the practice of kissing and using the same drinking utensils, all tend to form suitable means for the transmission and spread of the disease, especially when it is remembered that the bacilli may remain in the throats of children who have otherwise recovered perfectly from the disease and has been found in the throats of healthy children who have never had Diphtheria. Under those circumstances the importance of School life on the spread of Diphtheria is obvious. Moreover, it has been shown in London that during the Summer holidays there was a large

drop in the notifications of Diphtheria which was followed by a rise on the re-opening of the Schools .

Dr Thomas ,D.P.H. (B.M.Journal Aug 27.04.) in an Article entitled "School Diphtheria in the Metropolis" deals in a comprehensive and practical way with the spread and prevention of the disease in London Schools. In 29 Schools attacks of Diphtheria were investigated, and the following classes of children were found by Bacteriological examination to be spreading the complaint:-

1. Actual mild cases of Diphtheria in attendance 80%
2. Cases coming from infected houses but presenting no symptoms, 12%
3. Cases of recrudescence after absence for notified Diphtheria, 6%
4. Carriers without symptoms or demonstrable contact, 2%

It thus appears that mild cases in actual attendance at School are by far the most serious cause of School spread, and this is a fortunate circumstance, because they are easily detected. The method of investigation is interesting . The head Teachers report on a special form each case of exclusion for Diphtheria,the teacher stating which class-roomthe child attends, and the date of the last attendance. As soon as any suspicion of School influence arises the Schools are visited and those returns

examined, an explanation is required of all absences especially of children who have been away and returned after a few days. In any case of doubt the child is specially examined. Next, each child in the affected class is examined separately, and each case with clinical symptoms is set aside for bacteriological examination: to those are added all children coming from recently infected homes and children who have been notified as recently ailing by the Teacher. By swabbing selected children in this way the "Carriers" are usually detected and excluded and rarely does it occur that the disease continues to spread. If it does so a second visit is paid to the School, and each member of the class swabbed and examined.

This observer is adverse to School closure because he is of opinion that this is unnecessary where proper bacteriological diagnosis exists and because carriers would be undetected and continue to spread infection, and further that there is no guarantee that at the end of the closure period all Scholars will return free from infection.

The main points elucidated by perusal of this valuable paper are :--

1. Diphtheria is spread by Schools to a considerable extent,
2. It is spread by direct personal transmission,
3. It can be checked by swabbing and excluding children carrying Diphtheria bacilli,

4. Those children are chiefly mild cases actually suffering from the disease,
5. Their age is usually between 5 and 8 years,
6. Pseudo-baccilli may safely be ignored,
7. There is greater need to recognise the rôle played by contacts and carriers,
8. All contacts should be swabbed before being allowed to mix with the general population: Home disinfection without this is futile.

TRANSMISSION OF DIPHTHERIA BY MILK.

The bacillus of Diphtheria will live and multiply in milk at temperatures from 64-68° F. Exposure of milk therefore to the risk of contamination with the contagion may prove a means of conveying infection. It was in 1878 that actual proof was obtained of the dissemination of Diphtheria by milk by Mr W.H.Power (Report to Loc.Gov. Board Dec. 10. 1878). The incidence of the disease was very marked in persons who had consumed milk after its storage at the ordinary atmospheric temperature : this is attributed to the development and multiplication of the organism during the process of storage.

Cases of milk-traced Epidemics may result in two ways. in one class the contagion is attributed to a human source during collection and distribution of the milk. In another class to infection from Cows which suffer from an inflamatory disease of the Udder in the form of a vesico-pustular affection.

Klein (Rep.Loc.Gov.Board 1889) inoculated cows in the shoulder with a virulent growth of the Bacillus Diphtheriae as a result of which local visicles and pustules containing the germ, formed on the udder and teats. With matter taken from the udder vesicles and pustules Klein inoculated Calves, at the site of inoculation vesicles and pustules formed similar to those on the cows themselves. The calves fell ill and were killed and postmortem exhibited appearances like those found in the cows.

In the human being the bacillus has a marked local action contrasting strongly with the disease in cows where the bacilli injected in the shoulder appeared later in the lesions at remote parts. In two out of five cases which Klein injected the bacilli were obtained from the milk given by the animals.

Similar experiments conducted by Abbott of Philadelphia led to negative results he having been unable to demonstrate the germs in the resulting lessons, but such negative results can hardly carry so much weight as the positive results of such an experienced observer as Klein.

Klein found that cats which had accidentally partaken of the milk from the affected cows fell ill with Cat Diphtheria, and in which post-mortem he discovered the bacillus and lessons similar to those found in the cows.

more especially the Renal lesions.

In certain epidemics the specific organism has been demonstrated in milk believed to be the source of the outbreak, but it has not yet been found in the milk or in the udder lesions of the cows to which a definite epidemic has been traced. (Goodall, Eng. Medica: p.4.Vol.3.)

Reviewing the literature in reference to milk epidemics one is forced to the conclusion that no definite proof has yet been given where the milk was affected as it came from the cow. Osler (Princ. & Practice of Med. 2nd Ed. p.104.) denies the identity of the disease in animals and man and that the two are intercommunicable.

In the majority of cases where epidemics are traced to milk supply one must conclude either that Diphtheria prevailed in or near the Dairies or that contaminated water was used to wash the milk cans.

TRANSMISSION BY CATS AND BIRDS.

Cats suffer from Diphtheria , and cases are recorded where it is believed the disease was transmitted from Cats to Man. Klein has been able to infect cats by inoculation of the cornea and conjunctiva with particles of false membrane from Diphtheria patients. Thorne quotes an epidemic where Dr Turner,M.O.H. East Hants, found evidence that children may communicate the disease to cats.

At Petersfield, in Hants, the cats in a certain row of houses in which Diphtheria has been prevalent were

found to be ailing: their throats were swollen and there was a discharge from the nose and eyes.

As to the communication of the disease from cats to man the Report of the Local Gov. Board 1888-9 contains an instance which tends to support this. A boy fell ill and died of Diphtheria. After the first day of the illness he was sick and vomited, and the cat licked the vomit from the floor. In a few days it became ill and had to be destroyed. During its illness this catwas left out in the back yard at night, and a few days later a neighbouring cat became ill. This second cat was nursed by four little girls, and all developed Diphtheria - other sources of infection were said to be carefully excluded. The most that can be said of this case was that the evidence was merely presumptive. Osler does not believe that the so-called diphtheria of cats is identical with human diphtheria.

BIRDS similarly suffer from so-called Diphtheria, but all the evidence tends to show that it is a different disease to that which affects man. Loir & Duclaux record a case where a child suffered from membranous sore throat during an epidemic of "Avian Diphtheria". They obtained false membrane from the throats of birds so affected from which they were unable to cultivate the true Diphtheria bacillus but only that of Avian Diphtheria (W.Pasteur, Gibson's Medi-

cine Vo. 1.p.200) Stevenson (Jour.of Compar.Medic.1898) is of opinion that "roup" - the popular name for Fowl Diphtheria - is identical with human diphtheria.

Harrison (American Pub.Health Assocn.Dec.1903) and Guérin (Recueil de Med.Vetenaire Jan.15 Tom X p.20) deny this identity as does Professor Osler (Princ. of Med. 2nd Ed. p. 104.)

WATER DISTRIBUTION. So far as is known no outbreak of Diphtheria has been traced to a water supply. Klein states (Nature, Mar. 5th 1891) that the bacillus of Diphtheria is killed in a few days when kept a few days in pure water.

FAULTY SANITARY DISPOSAL OF SEWAGE OR REFUSE does not lead to epidemics, for the improved sanitary arrangements in the past 20 years have not, as is the case with Enteric Fever, led to less frequent outbreaks of Diphtheria. Doubtless, however, imperfect sanitary conditions predispose or aggravate diphtheria by lowering the general health of such as are attacked by the disease.

The digging up of old drains and cesspools have been credited with originating epidemics, but here also the sore throat which results will, in the presence of the diphtherial entity, predispose to the malady.

ASSOCIATION WITH OTHER DISEASES.

Diphtheria frequently complicates other Zymotic

diseases, and of these Scarlet Fever is the chief, but sometimes also Measles, Pertusis, Enteric Fever and Tuberculosis. The statistics of the Metropolitan Asylums Board show that Scarlet Fever attacks those convalescent from Diphtheria quite as often as Diphtheria attacks those convalescing from Scarlatina.

The statistics of the Municipal Hospital, Philadelphia, show that examination of the throat in Scarlet Fever Patients 10-33% will give cultures of Klebs-Loeffler bacilli (Welch & Schamberg Acute Contag. Diseases, p.610).

In many cases of Acute Fullicular Tonsillitis in children the existence of Diphtheria can only be certainly ascertained by a bacterilolgical examination.

RELATION OF THROAT CONDITIONS TO DIPHTHERIA.

There is practically a unanimous opinion among observers that certain throat conditions predispose to attacks of Diphtheria, and that those throat conditions, if met apart from cases of recognised Diphtheria, would certainly not be regarded as having any definite relation to it.

Such throat conditions may be either a catarrhal inflammation of the mucous membrane of the fauces and nose enlarged tonsils & adenoids or deep seated tonsillar scars. Mouth breathing such as one finds in children with enlarged tonsils and adenoids predisposes to an

attack from the Klebs-Loeffler bacilli in that, the nasal function being practically in abeyance, cold air, perhaps laden with the germs, is directly brought in contact with the tonsils and pharynx , thus tending to lower their resistive powers. The very structure of the tonsils, with crypts and lacunae, will also give lodging to the organisms - and in this perhaps lies the explanation why the first evidence of Diphtheria is so frequently found on the tonsils.

The local mischief which "sore throats" occasion undoubtedly provides a soil favourable to the reception and multiplication of the contagium: certain writers would go so far as to doubt whether, in the absence of an unhealthy or abraded mucous membrane the diphtheritic germ would affect successful inoculation: but when the tonsils are swollen and inflamed with the mucous membrane stretched and thinned over the deepened crypts and lacunae then we have a condition not far removed from what is practically an open wound.

C H A P T E R III.

SYMPTOMATOLOGY and CLINICAL HISTORY.

INCUBATION PERIOD. This varies from a few hours to four days, in rare cases may be as long as 14 days. The duration of incubation mainly depending on the degree of virulence of the bacilli and the resistive power offered by the tissues.

Certain Prodromata such as general lassitude, malaise headache with a feeling of nausea may be experienced occasionally vomiting and a feeling of general muscular soreness. Vomiting is by no means so constant as in Scarlet Fever. The pain and stiffness in the fauces at the angle of the jaw is comparatively slight and trivial compared with an ordinary tonsillitis, and this from a diagnostic point of view is a valuable clinical point.

FAUCIAL DIPHTHERIA is very insidious in its onset, the patient, generally a child, looks ill and refuses its food. Rigors are exceptional. The temperature is raised but not markedly so compared with other throat affections. The pulse is accelerated slightly but does not assume the very quick type of Scarlet Fever. On examination of the fauces there will be a general hyperaemia of the pharynx and tonsils. The tonsils are somewhat enlarged

and are most often the seat of the distinctive primary lesion. Small spots of exudate begin to appear on the inner aspect usually of one tonsil, or in the crypts. At this stage it is very difficult to distinguish between the true disease and tonsilitis without bacterial examination. The exudate increases and the different spots coalesce till a dense opaque yellowish grey membrane results at first easily detached but quickly reforming and becoming more adherent. In severe cases the process extends on to the uvula, soft palate, pharyngeal wall and may form a continuous sheet. The underlying mucous membrane is inflamed and swollen and from it a slight ooze of blood may take place. If the membrane be now separated a raw bleeding surface will be left behind. In about five days time the exudate decomposes and separates naturally and emits a peculiarly offensive odour. The membrane may reform after separation but in untreated cases may disappear before the fatal issue which occurs in 7 - 14 days from the onset.

The cervical glands are enlarged and with the progress of the local affection become tender and

more swollen, occasionally the skin and subcutaneous tissues of the neck are also swollen. The nasal passages are often invaded and a blood stained watery discharge may flow from the nostrils, occasionally nasal casts are expelled. The temperature falls somewhat after the initial rise and its subsequent course is very irregular; extension of the local mischief, the onset of adenitis, broncho-pneumonia or kidney involvement usually being associated with an increase of fever. During the last few days it may be subnormal from prostration. The pulse at first is moderately fast and of good volume, its rapidity depending on the amount of Toxaemia. Infants are specially liable to a rapid pulse rate. As cardiac failure increases the tension falls, the pulse becomes irregular and may fall in rapidity.

Albuminuria may be found on examination of the urine. Constitutionally there is pallor and prostration in severe cases becomes marked, the patient becomes drowsy, apathetic, and often vomits, the urinary secretion diminishes and death results from Asthenia. Delirium is uncommon. In mild forms of the disease again, the functional disturbance may be

slight, merely a sore throat with only a few patches of membrane and pain on swallowing. This may last for 6-8 days and apparent recovery ensue to be followed by paralytic phenomena. The exudate may not be membranous in character but assume a filmy pultaceous or gelatinous mass. The anterior pillars of the fauces are rarely the seat of the primary lesion, the posterior on the contrary are often so, here the exudate is often softer and moister looking and of greenish white colour.

In mixed cases (strepto-coccal and Loeffler)and in phlegmonous cases the whole throat is usually involved from the beginning, menbrane rapidly forms and is of a dirty grey or blackish colour, and is associated with oedema of the fauces and uvula, the cervical glands and tissues being also involved. Such cases show early and grave constitutional symptoms, high temperature, rapid feeble pulse and great prostration associated with frequent vomiting. Death takes place from cardiac failure, involvement of the air passages and general septicoemia.

Finally there are cases where the toxaemia is overwhelming and through the virulence of the associated

strepto-cocei the affected tissues may slough, recovery being exceedingly rare and only in treated cases.

NASAL DIPHTHERIA Next to the fauces the nose is the most common site of the diphtheritic process. It may occur by itself or be associated with faucical or laryngeal diphtheria. When the process starts in the nose and spreads backwards, the membrane is apt to be seen on the posterior wall of the pharynx and uvula. The primary variety may be met in infants. They are listless, have poor apetites, and show mal-nutrition. The temperature may be up one or two degrees. The infants breathe badly and this is of a snuffling character rendering breast feeding difficult or impossible. The nasal mucus membrane is reddened and swollen, a blood stained discharge issues from the nostrils which, by its irritation, causes excoriation of the nostril and upper lip with crust formation. In a few days a fibrinous exudation forms on the septum and spreads to other parts of the nasal cavity, occasionally casts of the choanae are shed with great relief to breathing, the children being again able to suckle, which they do eagerly, improvement may follow or

a return of the membrane. The mischief may not remain local but spread to the pharynx and give the clinical aspect already described along with the mechanical obstruction to breathing. A fatal result may result from suffocation in attempts at suckling or during sleep, or toxic symptons may end the scene. In older children similar symptoms are met with only as a rule less severe, high temperatures are common and the breathing snoring in character there being constant attempts to rid the nose of the impediment. Epistaxis results in some cases. From the free lymphatic distribution in the nose toxic symptoms are apt to be severe: and meningitis may result from extension through the cribriform plate of the ethmoid Vieillard (Jour de Méd et de cher. Pratiques Dec 10. 1903) points out the importance of coryza and epistaxi-is in diphtheria. Epistaxis appearing during the prodromal stage he regards as a grave symptom, haemophilic patients with diphtheria run a great risk from haemorrhage. The earlier the epistaxis the worse the prognosis, and in malignant cases it may be aninitial sign: His cases showing epistaxis gave a mortality of 70%.

In a series of six cases of early epistaxis collected

by Geyott (Thèse de Paris No 445) 5 ended fatally. The nasal symptoms of Diphtheria may closely resemble those of a foreign body in the nostril, the bloody ~~effusive~~ offensive unilateral nasal discharge being very suggestive of such, and where none can be found a bacteriological examination is desirable. Nasal diphtheria frequently runs a very protracted course the symptoms being a chronic rhinitis or catarrh and from the presence of the Klebs-Loeffler bacillus in this discharge those cases are a grave source of danger to others. The bacilli have been found capable of infecting others 63 days after the disease had apparently terminated --

LARYNGEAL DIPHTHERIA. In the great majority of cases this is secondary to faucial diphtheria, but as it may follow very mild cases the illness becomes recognized as diphtheria only after laryngeal trouble occurs. Laryngeal affection occurs in 11-15% of all cases of clinical diphtheria (Goddall Ency. Medica.vol.3.p.6) It usually shews itself within a week of the start of the primary affection. The symptoms are those of laryngeal obstruction aphonia, stridor, cough, and recession of the chest wall. In adults aphonia may be the only symptom of

extension to the larynx as the relatively large calibre of the respiratory tract allows of membrane being present without necessarily giving rise to obstruction. In a child suffering from faucial diphtheria change in the voice and an irritating cough usually indicate the trouble. Membrane may form so quickly after the start that the stenosis may become complete in 24 hours -- usually however the course is slower, examination of the throat and attempts at swallowing induce paroxysms of coughing. As the trouble advances towards obstruction the clinical picture is very striking. The patient becomes restless+perspires freely about the head and face: the cough avails little in relieving the dyspnoea, a little mucus at most being got rid of after a paroxysm in which the patient's eyes may bulge with the expiratory efforts Aphonia, partial or complete, rapidly developes, stridor occurs with inspiration, the breathing becoming whistling in character with a well marked pause between inspiration and expiration. The extraordinary muscles of respiration are called into play; recession of the chest wall and diaphragm become evident with

depression of the supra-clavicular regions. From time to time attacks of asphyxiation occur. The child sits up suddenly coughing with great violence the face is livid and anxious, the veins of the face and neck are swollen, the hands grasp at the throat in vain endeavours to clear away the obstruction, the little patient appealing helplessly to those about for relief. If unrelieved, Cyanosis increases, the surface becomes chilled, unconsciousness supervenes to be followed by death: should the attack subside the patient falls backward exhausted & bathed in perspiration. Relief sometimes is obtained by coughing up a piece of membrane. If a laryngoscopic examination be feasable there will be seen general oedema of the cords and epiglottis with membrane formation, the cords anteriorly being immobile, the edges in tact except posteriorly where a small chink exists.

In rare cases a cast of the Trachea and Bronchi is expelled during coughing giving great relief: should the disease improve before suffocation occurs the membrane is gradually separated and coughed up recovery ultimately ensuing.

CAUSES OF ASPHYXIAL ATTACKS. Several theories are advanced to account for those attacks. Spasm of the glottis, obstruction by false membrane, paralysis of the dilators of the glottis and poisoning of the respiratory centres by carbonic acid gas with reflex irritation of the pneumogastric nerve -- etc. It is not uncommon in children dying of laryngal obstruction to find little or no membrane about the larynx but only a congested and swollen mucus membrane. Further the attacks occur suddenly, often excited by slight causes so that it would appear there is a nervous cause at work causing spasm by contraction of the laryngeal muscles, that the attacks may be temporarily relieved by emetics and even by attempts at quietening the patient would go to support such a hypothesis and further it may be demonstrated during intubation that actual spasm may exist.

Important as is the spasm however in inducing this condition the production of false membrane on a swollen mucous membrane is an additional factor to be recognized especially in the later stages when the dyspnoea may continue after it might be

supposed that through fatigue the muscles would fail to respond to any to any stimulus. Pale Asphyxia (Asphyxie blanche) is a condition sometimes seen in the later stages of laryngeal obstruction. Normally the contraction of the diaphragm is co-incident with dilation of the glottis. In croup the latter is closed while the diaphragm contracts, air therefore, fails to enter the lungs in sufficient quantities to inflate them so that a vacuum is produced, hence the epigastric depression and recession of the intercostal spaces. The vacuum causes the blood to enter the intra-thoracic vessels thus depleting the peripheral vessels and causing the characteristic pallor, always a grave symptom demanding speedy relief to the obstructed repiration. The Pulsus Paradoxus which is sometimes observed in these paroxysms owes its explanation to similar reasoning; that is, on account of the partial vacuum in the Thorax the blood is drawn in to it from the peripheral vessels so that with each inspiration there is partial or complete obliteration of the radial pulse.

DIPHTHERIA OF THE TRACHEA AND BRONCHI.

This is generally the result of extension from the Larynx. Cases are recorded where the process was

apparently limited to the Trachea without any sign of Laryngeal infection. Occasionally the fibrinous exudation extends to the terminal bronchi. In Diphtheria following measles the disease may begin in the Trachea and bronchi and secondarily affect the Larynx. To this condition the name of Ascending croup is given. Bronchial diphtheria is very difficult to recognise unless a small cast of a bronchus be expectorated or signs of diminution of breathing be obtained over a certain area of the chest owing to blocking of a bronchial tube. Dyspnoea is marked and continuous, Cyanosis and physical exhaustion are common. Auscultation reveals numerous bruits and râles in the chest. The condition is very serious death occurring from Asphyxia or broncho-pneumonia, occasionally relief is obtained by the expulsion of casts of the bronchi through the mouth or after Tracheotomy and Intubation.

BUCCAL DIPHTHERIA In severe cases and especially in Strepto-Diphtheria extension of the false membrane takes place to the mucous membrane of the cheeks, jaws, and tongue. The false membrane is occasionally seen on the lips and corners of the

mouth. There is increased salivary flow, ~~is~~ foetid in odour and blood stained, the submaxillary glands are swollen and inflamed. Sometimes the disease begins in cracks about the lips, and later invades the inner aspect of the cheeks. The appearance resembles aphthous stomatitis, but the membrane is closely adherent. The staphalococcus is found in such cases in association with the Klebs-Loeffler organism.

CONJUNCTIVAL DIPHTHERIA. The conjunctiva may be the site of the diphtheric process resulting either from direct infection by means of the finger or by extension from the nose through the tear duct. The process may be catarrhal or membranus. Children are usually affected. Some previous inflammatory process in the eyes notably measles and granular lids may act as a predisposition to invasion. The whole structure of the lids may be stiffened by exudation into them impairing their motility. The ocular conjunctiva is rarely affected, Chemosis is usually marked: and a thin straw coloured discharge escapes when the lids are separated. This leads to redness and excoriation on the cheeks: The cornea may become weakened or perforated with prolapse of

the iris. The process may however not be destructive to vision in mild cases, but again severe cases may cause destruction of both eyes. The disease is commoner in Germany than other parts of Europe.

AURAL DIPHTHERIA. From a pharyngeal affection extension may take place via the Eustachian tube to the middle ear. Pain may be absent and the condition may be unrecognised till the drum ruptures and discharges pus. This discharge will show Klebs-Loeffler bacilli associated with strepto or staphalo-cocci. The Otorrhoea may persist a long time but rarely does permanent deafness ensue, though blocking of the Eustachian tube may lead to temporary deafness or it may result from a paresis of the muscles in the middle ear. - Emil Stangenberg (Nordist medicinsk Arkiv, Häft No.4 1902) found aural complications in 243 out of 1000 cases of Diphtheria. Otalgia was present only in 16 cases. Salpingitis of the Eustachian tube occurred in 190 cases. Exudative Otitis media was observed in 65 cases. The largest proportion of cases showed the complications after the first week. Stangenberg concluded that ear trouble was as likely to follow mild as severe cases of diphtheria: all his cases were slight in character on account of the antitoxin... ... .

which the patients received. This writer never observed a case of primary or secondary otitis externa diphtheritica in his 1000 cases. Connal (B.M.J. Jan. 19.07. p.139) reports a case which he considers primary diphtheria of the external auditory canal in which bacterial examination of the discharge from the pharynx and nasopharynx was reported "negative" but that of the patch of membrane which was situated in the external auditory canal was reported positive, after culture examination. Stangenberg (loc.cit) met with a solitary case of primary infection of the outer ear after publication of his 1000 cases. The occurrence however is rare.

CUTANEOUS DIPHTHERIA is not common even round the wound after tracheotomy - Cases of membrane occurring on abraded skin surfaces are recorded.

(Welch Schamberg p. 627) report a case where membrane appeared on the prepuce of a child who had developed diphtheria immediately after circumcision:

ANO-GENITAL DIPHTHERIA

The infection in this region occurs by direct infection from diphtheria elsewhere - and the infection is a mixed one. The vulva of little girls is the common site, less commonly the vagina.

These patches may spread to the anus and rectum. Swelling and redness accompanying the process and a blood stained discharge is a frequent associate. Pain is severe and inguinal adenitis results. In the worst cases gangrène of the parts may supervene. Freund (Zentralb.F.Gynäk. No.41 1905) records a case of Diphtheritis Vaginae during the puerperium in a young primipara, the process attacking a slight laceration on the posterior commisure. The case was associated with a rigor and high temperature. Bacterial examination detected the Loeffler bacillus associated with Streptococcus. The child died of nasal and faucial diphtheria after showing septic inflammation of the umbilicus. The temperature fell and the patient recovered under serum treatment. Several members of the family had the disease at the time.

Further consideration of certain symptoms met with in Clinical Diphtheria may be here considered in more detail.

TEMPERATURE In Diphtheria this is always irregular and rarely characteristic. In a mild case if a record be kept, there will be shown an initial rise

reaching its height as membrane is fully formed and then gradually declining though the Exudate may persist. Lennox Browne (Diph. and its Assoc.) states that in 1000 cases on an average, the temperature on the third day of the illness was 101° F. in 80 %, while in 50 % the average temperature during the course was below 99° F.

In septic diphtheria the fever is apt to be higher. Again in the most malignant cases it may be normal or even lower.

In acute adenitis complicating a case, a high temperature is to be expected and may reach 104° F. Where high temperature persists we may suspect some complication e.g. broncho pneumonia.

Laryngeal extension may be associated with a high temperature, in none of my cases did it exceed 103° F.

THE PULSE In many cases is not unduly rapid. In severe cases in children it may reach 120-160 per minute. The occurrence of Bradycardia after

subsidence of the acute symptoms is of grave import and if associated with Anuria and vomiting is invariably fatal in termination.

Tachycardia is common in infants and where there is nasal involvement, because of free absorption of the Toxines by the abundant lymphatics in the nose. Irregularity in force and rhythm is not always of grave import though there may be frequently indicative of serious myocardial change.

HEART AND BLOOD General enfeeblement of the heart and circulation occurs in all diphtheria cases and is part of the bodily exhaustion accompanying the disease. The cardiac sounds are weakened and the first shortened in length. The blood pressure is reduced as a result of Toxin absorption; marked reduction warrants a careful outlook. Babinsky (Welch and Schamberg p. 670) notes that there is increased coagulility - due to the action of the Toxins. This is liable to lead to Thrombus formation and may give rise to paralysis from cerebral embolism. Further this condition may lead to formation of cardiac thrombosis with symptoms of collapse, cardiac arrhythmia and syncope. In severe septic cases haemorrhages may result in various tissues... ... ...

owing to thinning of the blood and weakness of the vessel-walls.

The red cells are diminished to a certain extent as is the Haemoglobin but such diminution does not seem directly dependent on the gravity of a case. Myelocytes may be noted in films. Leucocytosis is marked as the disease increases, but decreases in convalescence. Where myelocytes are present and where leucocytosis is absent the prognosis seems to be bad otherwise the blood examination in diphtheria does not give us much valuable information especially in diagnosis.

URINE. The amount of urine passed is variable often normal, soemtimes diminished, Anuria more or less complete may occur and is very fatal.

ALBUMINURIA is so common as to become a symptom rather than a complication. It is said to occur in 50-75 % of the cases. (Ency.Med.Vol.3 p.74) Generally it appears early, usually on the 2nd or 3rd day. In mild cases it may be so small in amount as to escape observation. As a rule it is transient persisting to about the 10th day.

It is not always associated with evidences of Renal.

lesions its presence being due to irritation of the kidneys during excretions of the Toxines. Its presence may be taken as a rough guide to the severity of a case; the more persistent the albuminuria and the greater the amount, the more severe will be the case.

Odema is a rare accompaniment and is limited to the face - this may be due to an intense systemic poisoning apart from kidney lesions.

Casts-indicative of Renal damage, may be observed microscopically; hyaline, epithelial or granular, Blood cells are rarely seen (Park, in Amer.Sys.Pract. Med.)

Uraemic complications are less frequent than in post scarlatinal nephritis.

TOXAEMIA A peculiar train of symptoms results from absorption of the Diphtheria Toxins. These may make their appearance after the disappearance of the exudate in the 2nd week of the illness; the patient may when apparently going on well, suddenly show vomiting with intolerance of food. Pallor becomes marked, the pulses irregular and often slowing down to 50 beats. As the Toxaemia progresses the

surface temperature falls, the limbs get cold and livid, and the expression anxious. When not too profound recovery may follow, though the patient is in constant danger of sudden cardiac failure: or again, the condition may be progressive and death result gradually from heart failure preceded by precordial pain and vomiting: consciousness is usually retained to the last.

BURROWS (Amercian Jour. Med.Science Feb. 1901)gives a clinical review of 2,093 cases of diphtheria, which is of interest and may be briefly reviewed as to:-

1. SITE OF MEMBRANE

Both Tonsils		in 1528	cases
One Tonsil		in 243	"
Uvula		" 404	"
Posterior wall of Bharynx			173 cases
Palate	"		244 "
Nostrils	"		71 "

2. PRESENCE OF BACILLI.

In throat alone		in 944	cases
"	Nasal Secretion	790	"

Absent in 228 cases of which 71 were fatal from well marked clinical diphtheria.

3. COMPLICATIONS

(a) Cardiac disturbance was noted in 65% of the cases a systolic murmur in 984 cases, irregularity in 658 and bruit de galop in 22 cases.

(b) Albuminuria was present in less than 1/3 of the cases tested, in 205 cases testing was impossible.

(c) Laryngeal involvement occurred 337 times.

Intubation was necessary in 213 cases with a mortality of 45 % Tracheotomy was performed after intubation in 3 cases all of which were fatal.

(d) (d) Adenitis (cervical and submaxillary) occurred in 1058 cases.

(e) Otitis Media in 61 cases.

(f) Paralysis) Palatal in 72 cases.
) Oculo-motor in 19 cases.

(g) Scarlet Fever was superadded in 25 cases.

4. FATAL CASES causes

Toxaemia 172 cases

Degenerations of Tissues 54 cases

Pneumonia 14 cases

Mixed Infection Death rate 31.3 %

5. ANTITOXIN was used in all cases average dose 4000 units every four hours. Death rate in uncomplicated cases, exclusive of those moribund on admission was 9%

6. AGE Under 15 years 1647 cases, of which 14 % died.

Over 15 years 315 cases, of which 2.85 % died.

C H A P T E R. IV.

THE COMPLICATIONS AND SEQUELAE OF DIPHTHERIA.

PARALYTIC PHENOMENA form perhaps the commonest and most striking of the complications and sequelae of Diphtheria. Very little seems to have been known of this subject prior to the latter part of the 16th century. Nicholas Lepois called attention to it in 1580 and Heredia (Sanné-Diphthérie p 6) records cases of paralysis of the palate, pharynx and limbs during an epidemic at Spain at the beginning of the 17th century. Herrera (Greenhow Diphtheria p 18) a contemporary of Heredia alludes to the peculiar sound of the voice which he compared to that found in Syphilis. A definite relation between the faucial attack and subsequent paralysis was not demonstrated before the middle of the 18th century. Chomel dealing with an epidemic at Paris 1748, Ghisis with that at Cremona 1749, and Bard with that in New York 1789, each describe cases. In 1854 appeared a paper on diphtheritic paralysis by Maingault (De la paralysie du voile du palais à la suite d'angine) in which he made note of the nasal voice, the regurgitation of fluids by the nose, the anaesthesia and immobility of the velum

palati. Maingault was followed by a number of other observers, Trousseau in France and Jenner and Greenhow in this country. Up to 1862 Trousseau regarded the paralysis as a pure coincidence, but in that year he had a case of generalised paralysis following a faucial attack which led to his further observations on the subject. He described two forms, one malignant rare and always fatal with respiratory affection, vomiting and convulsions, the other mild and ending in recovery (Clinique Médicale de l'Hôtel Dieu de Paris Vol I pp 494-521) The first Histological investigations on Diphtheritic paralysis were made by Charcot and Vulpian (Comptés rendus de la Société de Biologie 1862.) They showed in a fatal case of palatal paralysis the motor nerves alone were affected consisting of tubules devoid of medullary substance, the Neurilemma containing numerous granules. The sensory nerves showed no change. Fatty changes were present in a few muscle fibres. After the discovery of the specific organism in 1883, fresh observers took up the subject. Roux and Yersin (Annales de'l'Institute Pasteur 1888-1889) produced the characteristic sequelae in animals by injection

both of the bacilli and their toxines.

FREQUENCY of OCCURRENCE. At the Eastern Hospital during 1892 and 1893 before the introduction of Antitoxin treatment, paralysis occurred in 12% of all cases. (Ency. Med. Vol.3.p.8), Lennox Browne in 2848 cases treated at the various Hospitals of the Metrop. Asylums Board in 1893 gives the percentage at 14%. The percentage occurrence at the hospitals of the Metrop.Asylums Board for the years 1895-1902 varied between 20. 4% and 15%. It is somewhat difficult to collect exact statistics on this subject for various reasons eg. its presence in young children is often missed, slight cases may be overlooked, many patients after convalescence is established pass from observation and any subsequent paralysis may be so slight as not to attract attention, lastly paralysis incidence since antitoxin was introduced is slightly higher then before, the explanation most likely being, that more cases are tided over the acute stage of Diphtheria and are spared to be exposed to the risks of paralysis.

THE CAUSE AND PATHOLOGY of Paralysis in Diphtheria are not definitely known. It would seem that the condition is probably a Toxic Neuritis involving the

peripheral nerves causing an interruption of the nerve supply to the muscles concerned. Fatty change may result in the muscle fibres, as has been referred to in connection with the Myocardium. Anatomical changes of a myelitic nature have been found in the Cord; and by some writers, this is regarded as an important element in the production of paralysis.

RELATION OF AGE AND SEX according to Woollacott (Lancet 26 Aug.1899) males and females are equally affected. Though all are agreed that the greatest incidence of Diphtheria is upon ~~the~~ the young the same unaminity does not prevail as to the relative frequency of paralysis at different ages. Woollacott (Loc.cit.) is of opinion that paralysis affects young children more than adults, and he points out how it is apt to escape notice when occurring at an early age. Osler (Princ.& Pract. of Med.p.116) says, on the contrary, it is less frequent in children than adults. Herringham (Allbutts System of Med.Vol I) says he found many out-patients with paralysis who had been discharged from the Hospital as cured.

RELATION TO THE CHARACTER of the initial attack Here again a great diversity of opinion exists.

Trousseau(Loc. cit.) admits paralysis is more common after severe attacks, but that mild cases are not exempt. Greenhow (loc.cit.) Wilks (Clin.Lect on diseases New System) are of opinion that no proportion exists between the subsequent paralysis and the character of the faucial involvements. Jacobi (20th Cent. Pract. Vol.XVII) and Henoch (Dis. of Children New Syd. Soc.) go so far as to assert that mild attacks are more liable to be followed by paralysis than severe. Goodall (Brain 1895) and Woollacott (Lancet 1900 and Metropol Asylums Board Reports 1898) hold exactly opposite views viz: that the same severe attacks of diphtheria are more liable to be followed by paralysis.

While we must admit that mild diphtheria is frequently followed by paralysis and indeed that paralysis may follow cases of"sore throat" which were never recognised as diphtheria as in an ambulatory case quoted later which came under my observation, Still I believe the majority of observers are of opinion that paralysis is most liable to ensue after a severe initial attack. The opinion of Goodall and Woollacott, who are on the Staff of

The M.A.B. Hospitals, must carry great weight from their extensive experience. The discrepancy of opinion may be partly due to certain cases where no pain was complained of in the fauces being regarded as mild which were really of a severe type, some of which may have suffered from Toxaemia with absence of pain on this account. Another source of probable error lies in the fact that in Hospitals for Infectious diseases mild cases of Diphtheria would be kept at rest in the recumbent position and so might escape paralysis whereas mild ambulatory cases might, under the less favourable conditions, (absence of rest) develope paralysis and thus be seen in private practice more often than in Fever Hospitals.

We must conclude then that paralysis is relatively more frequent after Faucial Diphtheria and also after a severe attack. Purely Laryngeal Diphtheria, I believe most are agreed, is rarely followed by paralysis but pure Laryngeal diphtheria itself being comparatively rare we must not be surprised to find paralysis following cases after tracheotomy where there existed concomitant faucial exudation.

RELATION OF PARALYSIS TO ANTITOXIN. Marfan (Clinique Infantile Hospital des Enfants Malades Paris) asserts that since the introduction of serum treatment paralysis has greatly diminished. This statement must be accepted with reserve. It is supported by M.M.Weill & Dequy (Traitement de la Diphtérie 1902)who have met with less paralysis of the limbs, eyes and viscera since serum introduction The best statistics are furnished by the Metrop. Asy. Board. In 1893 (pre-antitoxine year) the percentage of paralysis was 14.2, whereas in 1895 when serum was generally used the percentage paralysis was 20.4The probable explanation of this is given above.

The early administration of Antitoxin however makes paralysis less likely to ensue especially in a severe form. Woollacott's statistics M.A.B. Reports 1898 clearly establish this important point. This writer (Lancet 26th Aug.1899) shows that large doses of serum 4000 units and upwards are more effective than small doses in preventing paralysis and lowering its mortality. The doses of antitoxin given at the Metrop.Asy. Board Hospitals exceed as a rule those given elsewhere.

RELATIVE FREQUENCY OF THE DIFFERENT FORMS OF PARALYSIS. The palatal affection predominates in frequency, followed by paralysis of the oculo-motor

muscles of which ciliary palsy is more commonly seen than any variety of ophthalmo-plegia externa. Goodall (Ency.Medica, Vol III page 8) gives statistics of 125 cases observed by him as follows:-

SITE	Cases
Palate appeared	102
Ciliary muscles affected	56
Legs affected	52
The external ocular muscles	26
The arms affected	21
The Larynx affected	14
The Diaphragm affected	10

In this series also,

28 cases remained limited to the Palate

17 " " " " " Ciliary Muscles)
11 " " " " " Palate and Ciliary muscles)
6 " " " to the Palate and " Legs
3 " " " " " Palate and Ocular muscles
1 case " " to the Respiratory muscles)

Time of OCCURRENCE AND MODE OF ONSET.

Diphtheritic paralysis generally sets in during the latter half of the second week or during the third

or fourth week. The first signs generally noted are a nasal twang of the voice and regurgitation of fluid through the nose on deglutition. If such a case be examined the soft palate will be found insensitive and motionless. Different cases vary in the extent shewn by the lesion. Frequently the palate will be the only part affected or loss of accommodation in addition may be observed the patient reading or threading a needle with difficulty. Sometimes internal strabismus will result from paresis of the external recti muscles. Diplopia may be complained of. Bolton (Lancet Dec.13. 1902) recorded two cases of optic Neuritis occurring 3-4 weeks after an attack of diphtheria. In both recovery ensued. Optic Neuritis is a very rare complication.. Other cases again later in the disease will complain of tingling sensations in the limbs usually the legs followed by a condition not of actual paralysis but paresis in the extremities involved, so that both sensory and motor nerves may be affected. Yet again in other cases the trunk or neck muscles will be affected and sometimes the respiratory muscles, bladder or rectum and last of all the dreaded cardiac paralysis may ensue.

Paralysis of special senses is rarely observed.
In generalised cases paresis rather than paralysis is the rule: the loss of muscular function being rarely complete and even varying from day to day.
Palatal paralysis usually ensues about the end of the third week, unless in very severe cases when it may appear much earlier, such patients are rather liable to cardiac paralysis the condition indicating a severe toxaemia of the nervous system.
Fatal cardiac cases ushered in by vomiting and restlessness are apt to supervene in the first fortnight. The eye affections generally begin later than the preceding paralysis. Paralysis of the muscles of the limbs may not supervene till the 5 or 6 weeks or later. The duration of the paralysis varies considerably. Palatal palsy may last about three weeks. Eye affections rather less.
Diphtheritic paralysis may bear a close resemblance to Syphilis. The frequent affection of the ocular muscles, the fluctuating character, the liability to follow an untreated lesion all tend to simulate cerebral syphilitic lesions.
Diphtheritic palsy however follows as a general rule more quickly on the primary lesion than do

syphilitic palsies.

The following case which came under my notice a year ago will serve to illustrate some of the points connected with diphtheritic paralysis.

J.W. Male, Aet. 22 years, Boiler worker - while engaged at his work in Lincoln, he had a slight sore throat, of which he took little notice and was not obliged to desist from his occupation He was seen by a medical man at the time who, however, apparently saw no reason to suspect a Diphtheritic infection. He had no serum injected but was given a gargle: the throat recovered in 10 days time. Three weeks later he began to notice a tingling sensation in his feet and legs with weakness of his knees. He was obliged to leave work and return to his home in Newark. When I saw him his condition was one of partial paralysis of his lower limbs, the knee jerks were much diminished on either side, cutaneous sensibility was impaired below the knees and especially on the outer aspects of the leg. He was a man of strong physique but exhibited flabbiness in his calf muscles. The gait was staggering in character his knees tending to give

way beneath him. He never had any regurgitation of fluids through the nose and did not know of any alteration of his voice. Nor was movement of the palate defective. He had noticed however some difficulty with his work from bad eyesight and near vision was found very defective. He had a slight tendency to Nystagmus on turning the eyes to either side. He was treated with massage. Large doses of strychnine and nourishing food, and after nine weeks treatment made a complete recovery the ocular condition improving and disappearing first.

Here was a case of mild unrecognized diphtheria of an ambulatory type, which on the 30th day after his illness began showed a form of paralysis affecting his lower limbs. The date of onset of his eye condition could not be acurately ascertained as the nature of his occupation did not demand very much accommodative power. After somewhat prolonged treatment recovery was complete.

The following case which I saw with a brother practitioner was of a much more serious nature. F.W. aet. 8 years, female, had "sore throat and fever" for three days before I saw her first, but as there

was no known epidemic in the town the parents thought little of the illness except that the child did not get better like an ordinary "sore throat" The palate and tonsils showed abundant membranous exudate. The Temperature was 100.8° F. Pulse 118 per minute. The urine showed a trace of albumen. The case was then seen by a Dr. B. as I had an important confinement imminent. She was given 1000 units antitoxin, this was repeated only once on the following day as the membrane quickly began to disappear and the temperature fell to normal. All appeared to be going on well when at the end of a fortnight the palate showed signs of paralysis indicated by a nasal voice and some trouble in swallowing fluids. In the middle of the fourth week when the child was allowed to sit up it was noticed her legs were very weak, the knee jerks were absent but sensation was not much impaired. The gait was staggering in character but the child was scarcely able to walk at all. A week later signs of diaphragmatic paralysis became evident, the child's condition being critical The breathing was almost entirely thoracic, the abdomen being practically immobile except for an

indrawing of the epigastric and hypocondriac regions during inspiration. Breathing was embarrassed and accelerated with slight Cyanosis, numerous rhonchi and crepitations were present over the bases of the lungs, coughing was rendered difficult from the absence of diaphragmatic contractions during the effort, instead of their being a sudden expiratory effort, this was replaced by a slow straining movement attended by considerable efforts on the patient's part. The paralysis was apparently bilateral. The child was so weak she could not voluntarily change her position in bed, the evacuations of the bowels were difficult to manage on account of the paralysis of the diaphragm. Fortunately the intercostal muscles remained unaffected. She was treated by strychnine internally, massage and ~~electrode~~ faradism, one electrode being applied to the phrenic in the neck and the other to the epigastrium. Recovery was long and tedious. The child showing great emaciation, but was ultimately after fifteen weeks treatment, complete, the diaphragmic condition recovering long before the legs regained their complete function. McKenzie (Intercolonial Med. Journal Nov. 20. 1901) reports two cases of Phrenic

paralysis, the first setting in suddenly with alarming symptoms following the administration of a dose of medicine. The face became congested and the expression anxious, there was Dyspnoea the respirations being of a catchy embarrassed slow nature. The pulse was 100 regular, of poor volume and tension - the extremities were cold. The whole picture resembled one of pulmonary embolism. The speech suddenly became a mere monosyllabic whisper, prior to the attack the voice had been strong and articulation distinct. The abdomen was carcinated and moved in a jerky spasmodic fashion, pneumonia followed in a few days and the child died of cardiac failure on the sixth day from the onset of the palsy. The second case showed practically the same signs, especially the whispering voice. The child died of cardiac failure on the fifth day. In this case beyond an untreated faucial inflammation three weeks previously no accurate history was obtained of Diphtheria.

McKenzie lays great stress on the characteristic monosyllabic voice in cases of diaphragmatic paralysis. In my own case the voice though nasal and weak was not reduced to a whisper at any

time of the illness.

Paralysis of the Pharynx and deglutition in Diphtheria are not uncommon and lead to difficulty with feeding and risk of food entering the larynx and perhaps leading to septic pneumonia if care be not exercised in feeding. Infants may die of starvation through inability to suckle in this condition, and adults show great emaciation often in spite of rectal feeding.

Facial paralysis has been observed in Diphtheria but is of comparatively rare occurrence or is obscured and missed owing to the attention being more urgently called to other parts.

Cardiac Paralysis is referred to under cardiac complications: Hemiplegia is but rarely seen in Diphtheria. There are 35 cases in all recorded. The post mortem appearances in those examined being in one case a lenticular haemorrhage pressing on the internal capsule, the other five showed embolism of the sylvian artery. In the 35 cases there was complete recovery in 4, death in 7 and in the others more or less paralysis.

(Welch+Schamberg Ac. Contag. Dis. p.647) Tendon Reflex Paralysis as exemplified in the knee jerks is a common accompaniment of Diphtheria and may be present from the first or be preceded by a stage of

exaggeration (Gibson's Medicine p.210) It is also of long duration the normal reflex only returning after an interval of several months.

DIAGNOSIS OF DIPHTHERITIC PARALYSIS. Slight degrees of paralysis are very liable to be overlooked and a close watch should be kept for any signs indicating the various forms during an attack of diphtheria. The sound of the voice, the mobility of the palate and the accommodative power as tested by test types or threading a needle or beads in children, should be examined frequently, also any tendency to squint at any time of the day. The importance of recognition of the slight degrees lies in the fact that serious forms may in a day or two follow. For instance a slight palatal paralysis may precede involvement of the pharynx and diaphragm

CARDIAC COMPLICATIONS The poison of diphtheria is especially prone to affect the heart. Signs of cardiac failure are not common in the early stages of the disease, but if they occur during the first two weeks in severe cases are apt to be very formidable. They do not generally appear

before the end of the first week but during the succeeding four or five weeks are constantly to be watched for and guarded against. In severe cases of diphtheria fatty degeneration of the myocardium may be evident but undoubtedly also cardiac failure is not infrequently due to paralysis of the cardiac nervous mechanism. Jacobi (20th Century Pract. of Med) says " there is no case ever so mild apparently which may not affect the heart's function at once to a certain extent." From mild cases to the gravest there are gradual transitions.

The symptoms do not differ from those of Toxaemia. Vomiting is often a prominent and early sign. The patient may be pale, sallow or livid and cyanotic. The pulse at first may be rapid and feeble but eventually becomes slow and may fall to 40-50 beats per minute. It may also exhibit a gallop-rhythm at one time and not another. The heart may show signs of dilatation with the apex displaced outside the nipple line, increased cardiac dulness, and the first sound weak and indistinct. The extremities may be cold. The symptoms in some cases show a markedly fluctuating

character appearing perhaps at one time of the day and absent again at another. Marked inequality of the pulses may be observed at different times. These temporary improvements are deceitful as they are apt to foster false hopes of a good result whereas they generally herald a fatal termination . Death may result ffom Asthemia or sudden syncope. The following case will illustrate some of these points.

G.B. Female Aet, 5 years: First seen May 25th 1905 Died June 5th 1905. The illness began on May 22nd three days before the child was first seen when she had sore throat, headache and had been sick. On the 24th she had a nasal discharge and swollen glands in the neck. On examination membrane covered the tonsils and soft palate. The breath was offensive and there was a foetid nasal discharge. The cervical glands were enlarged on both sides and the urine showed an albuminous cloud. She was given 2000 units antitoxin at once, and this was repeated on five subsequent occasions. She refused food and was fed by the rectum with peptonised milk enemata, the fauces were syringed with carbolic acid solution 1 in 200,

On the 27th the throat was clearer, less foetor was observed, and the color was good, heart normal. Two days later small petechiae were present on the neck and abdomen and back where the injections had been made. In the evening the patient was restless and slight irregularity of the pulse was present. Heart sounds distinct and not rapid. By May 30th the membrane had disappeared from the throat and the pulses were equal and regular and of good strength. On June 3rd the patient retched and vomited, her color changing to ashen grey, the pulse was weaker and the cardiac first sound less distinct and not so loud as the second sound at the apex. Strict rest was enjoined and small doses of strychnine administered every three hours - June 4th vomiting recurred frequently, and the voice became distinctly nasal. The heart sounds were intermittent and the pulse showed a galloping rhythm at times - the apex beat being outside the left nipple line. The temperature had fallen to 97° F. In the evening the pulse was more regular and stronger, and the first sound was improved in strength but the apex beat was still in the same place. On the 5th June vomiting was again

troublesome, the pulse resumed the galloping rhythm, the heart sounds became very weak, the limbs cold and livid and death occurred the same night.

TERRIEN (Rev. des Malad. de l'Enfance Dec.1904) draws attention to the conditions in which sudden death may occur in Diphtheria. In his opinion sudden death is rare in children but nevertheless occurrs in such diseases as Diphtheria, Typhoid, and severe Toxaemia. It is difficult, he says, to form any idea from the nature of the cases whether or not a fatal ending may be expected. He quotes cases treated by serum in which early and rapid disappearance of the membrane warranted the expectation of an uninterrupted recovery, but which however, is not always realized. Terrien wishes particularly to warn us against attaching Undue importance to the absence of such signs as altered rhythm and rate of hearts action, vomiting and depression, as he has met cases in which no alteration of the heart's action could be detected and which died suddenly during what was apparently normal convalescence from Diphtheria.

The following cases support Terrien's opinions:-

C.B. aet. 5, Female: had an apparently mild attack of Faucial Diphtheria: She had 4 injections of serum 1500 units on each occasion. Convalescence seemed established and all well when during the 2nd week of the illness the child asked her mother for a doll to play with, the mother was sitting on the edge of the bed dangling the doll about when suddenly the child snatched at it, fell back, and died in a few minutes. In another case under my care at Lincoln Hospital a child of 18 months was admitted with Phimosis and was duly circumcised - a few days after the child without apparent reason developed a temperature of a little over 100° F. but was not obviously ill. Two days later the child suddenly sat up in its cot in the morning and fell back dead. A swabbing from the throat revealed the Klebs Loeffler bacilli, and a slight attack of Diphtheria occurred amongst other children in the ward. No. p.m. was obtained.

White and Smith(Boston Med. & Surg. Jour. Oct.20 1904) give 946 cases of Diphtheria with special reference to cardiac complications. 70% of their

cases were under 10 years of age and 10% ended fatally. They regard a pulse rate of over 140 as unfavourable, otherwise they rely little on the pulse as a prognostic guide - 2/3rds of their cases had regular pulses and over 90% of the cases distinct cardiac murmurs - systolic and apical. Definite cardiac enlargement was infrequent. These observers divide the cardiac complications met with into three groups. (1) The commonest exhibited a gallop-rhythm, vomiting, epigastric pain and palatal palsy, a Syndrome which they suggest may point to a vagus neuritis rather than a myocardial change. The majority of such died.

2. Where Tachycardia persisted for months and was easily excited by exertion.

3. A few showed a rapid fall in pulse rate sometimes from 110 to 30 or even 20 beats per minute with weak heart sounds prostration and death.

Their main conclusions may be summed up as follows:

(a) Murmurs and arrhythmia are frequent and not of themselves important.

(b) The rhythm of the heart changes so quickly that frequent examinations are necessary.

(c) Gallop-rhythm, vomiting and epigrastic pain are important and unfavourable complications.

(d) The heart needs special watching during the 2nd and 3rd weeks.

(e) Antitoxin prevents and does not produce cardiac complications.

(f) Prolonged rest in bed is necessary in all severe cases and care is necessary where arrhythmia or a murmur is present.

RESPIRATORY COMPLICATIONS Faucial diphtheria does not usually lead to serious lung trouble, but in the Laryngeal and especially the Laryngo-tracheal form lung troubles constitute serious dangers. Bronchitis is rarely absent in such and the false membrane may extend downwards and involve the bronchial tubes. Catarrhal Broncho - pneumonia is also of frequent occurrence and renders the outlook very grave. It is revealed by physical examination and the bases are most likely to be involved. A septic condition may arise from entrance of food particles into the larynx during deglutitation where paralysis of the pharynx is present. Collapse of Lung tissue may also result from occlusion of the small tubes: (case vi) Broncho-pneumonia is the main cause of

death after tracheotomy. Pleurisy and Lobar pneumonia are rarely met with.

LYMPHATIC GLANDS The cervical and submaxillary glands are commonly enlarged in Diphtheria and in septic cases are liable to break down and suppurate.

ZYMOTIC DISEASES. Scarlet fever though often associated with Diphtheria can scarcely be called a complication, 10-33% of scarlet fever cases may show Klebs-Loeffler bacilli in their throats (Welch and Schamberg, Ac Contag. dis. p.645) Cases of Scarlet fever may moreover during their convalescence be attacked by well marked Diphtheria. The important practical deduction from such facts is that cases of scarlet fever, may on their discharge from Hospital introduce diphtheria into their homes the patients not being known to suffer from Diphtheria during their stay in Hospital the one disease obscuring the other.

Measles and Diphtheria may also be co-existent or diphtheria may be a sequel to an attack of Measles - the relationship probably being of an indirect nature in that damage is inflicted on the mucous membrane of the throat and upper air passages by the measles thereby rendering the

patient susceptible to the infection of Diphtheria In such cases the disease is likely to assume a serious laryngo-tracheal form and to be complicated by Broncho-pneumonia.

ANAEMIA is a frequent sequel to an attack of Diphtheria.

RELAPSES occur in about 1% of the cases (Goodall Ency.Med. Vol. 3 p 9) and second attacks at various periods after the primary illness are not uncommon: so that the disease confers little if any real immunity from another attack.

THE TONSILS DURING CONVALESCENCE from Diphtheria are commonly the seat of a non-specific inflammation which is of little importance,-- sometimes a late Tonsillitis in the disease proves to be scarlatinal in origin and yet again Tonsillitis occurs during 2-3 weeks after serum injection and is associated with the erythematous rashes joint pains etc. met with under similar circumstances. The faucial affection or"angine de retour" of the French has been designated Angina redux. This is typically met with 10-15 days after injection (Sevestre et Aubertin, La Pédiatre pratique 1903 No.2:) The appearances vary from

an injection of the fauces with a tonsillar deposit to large semi-confluent patches resembling the early stages of Diphtheria. Unlike Diphtheria however they are not adherent. Bacteriological examination reveals rich growths of staphalococci and streptococci which accords with the theory that late manifestations of serum are due to these organisms (Sevestre et Martin in Comby's Traité des maladies de l'enfance Article on Diphtheria 1904) The condition though uncommon may be overlooked or taken for a relapse. The statistics of the Metropl. Asyl. Board Reports 1899-1904) give the average percentage of occurrence as 1.61: Sevestre and Martin (Loc.cit.) have recorded the necessity for intubation where laryngeal symptoms were present and which have been attributed to laryngeal oedema produced by the serum.

C H A P T E R. V.

MORBID ANATOMY AND PATHOLOGY OF DIPHTHERIA.

With the exception of the false membrane there are few Macroscopic changes found after death. As a rule the membrane is to be found on the Tonsils fauces and contiguous mucous membrane, at other times it is confined entirely to the Larynx and Trachea, or to the nose. The membrane may sometimes be traced into the larger bronchi as in one of my fatal cases after Tracheotomy. The consistence of the membrane varies, at times it will appear as large flakes and again as a friable pultaceous mass. It is more adherent as a rule in the fauces than in the larynx and trachea. Sloughing of the Tonsils may be found in severe cases. If the false membrane has been seperated before death has occurred, a granular appearance is left where it existed. The structure of the membrane has been already described, as consisting of a fibrinous network enclosing masses of dead epithelium and leucocytes.

VISCERAL CHANGES

ALIMENTARY SYSTEM. Swelling of the solitary glands in the intestine and of Pyer's patches may occur but no ulceration. The spleen is enlarged firm and

shows Hyaline changes in the vessels and cloudy swelling of the cells. The Liver also may show cloudy swelling of the cellular elements. Haemorrhage may occur in mucous membranes and solid organs as in other poisons.

HAEMOPOIETIC SYSTEM The cervical and sub-maxillary glands are frequently enlarged and may present Foci of suppuration. The Bronchial glands may also be enlarged where there have been pulmonary complications.

CIRCULATORY SYSTEM The Right heart often contains clots more or less adherent according to the rate at which death has taken place.

Endocarditis and pericarditis are rare except in malignant cases where ulcerative endocarditis may be associated:

Changes of a fatty or granular nature in the myo-cardium are not uncommon especially where death is due to cardiac failure. One of the most important studies of the heart in Diphtheria has been furnished by Romberg (Deutsche Archiv F. Klin. Med. 1891 Bd XLVIII) who carefully examined 8 cases. He found the cardiac muscle was not uniformly affected but that some portions may be normal and other areas show extensive change. The left heart was most affected.

Small foci of leucocytic infiltration were found

round the small coronary arteries along with myocardiac degeneration, the affected fibres had a peculiar vacuolation in the centre and were without nuclei. The inner and outer portions of the myocardium showed most degeneration. Pericarditis was present in 5 cases and endocarditis in 3 cases. In death from asphyxia in Diphtheria the Right cavities are distended with blood and clots and superpericardial ecchymoses are not infrequent.

RESPIRATORY SYSTEM. In addition to false membrane which may occupy the pharynx, larynx trachea and bronchi, puriform material may be found in the smaller bronchi more especially in deaths after tracheotomy. Patches of collapse and bronchi-pneumonia are of frequent occurrence.

When diaphragmatic paralysis has existed before death, collapse of an entire lobe of the lung may be present, the Right lower lobe being more prone than the others to be affected thus.

Subpleural ecchymosis may be noted. The bacillus has been cultivated from the contents of the lung alveoli when broncho-pneumonia has been present (Kutscher, Welsh and Schamberg ac.Contag. Dis. P 617)

but the pneumo-coccus is the principal agent in producing the lung affection.

URINARY SYSTEM.

The kidneys may merely show cloudy swelling of the cells, sometimes where Albuminuria has existed ante mortem they exhibit no changes, or they may be found in various stages of parenchymatous inflammation.

Mario Flammini (It. Policlin. Sept. 1904) describes in 11 cases the naked eye and microscopic appearances of the kidneys after death. He deduces from these studies that the kidneys are almost always damaged by diphtheria - and that the degree depends on the severity of the attack, the renal changes being proportional to the severity of intoxication. The changes fall mostly on the renal parenchyma where the cells are swollen and granular and the neuclei stain badly. Haemorrhages are very rare. In mild cases (fatal through some accident) changes may be confined to the Epithelium of the convoluted tubules; in more severe cases the changes involve the ascending and descending limbs of Heule's loop and in the most severe of all the glomeruli may be affected. The collecting tubules nealy always remain unaltered.

Flammini finds such changes agree with his clinical observations on urinary sediments during life. It is apparently then, mainly by the epithelium of the convoluted tubules, that the Toxin is excreted. Flammini suggests that where the glomeruli are affected it is due to some non-diphtheritic micro-organism circulating in the blood.

NERVOUS SYSTEM.

Fatty Degenerative changes have been found in the Medulla, spinal cord and nerves. The concensus of opinion is that the nerve changes are mainly responsible for the paralytic phenomena. The changes which bring these about affect sensory and motor and sympathetic nerves and consist in a breaking up of the axis cylinder into globules followed by similar changes in the substance of Schwann.

THE SKELETAL MUSCLES may exhibit varying degrees of fatty change in cases where the cardiac muscle is thus affected and also where degenerative changes are noted in the peripheral nerves.

CHAPTER. VI.

BACTERIOLOGY OF DIPHTHERIA.

In the year 1891 the requirements of Koch concerning the specificity of the Klebs Loeffler bacillus had been fulfilled , its constant presence in cases of the disease its isolation and culture, the reproduction of the disease by inoculating animals with pure cultures and the presence of the bacillus in the artificially induced disease all demonstrated beyond doubt that the bacillus of Klebs Loeffler was the cause of Diphtheria.

MORPHOLOGY The bacillus is rod shaped, straight or slightly curved non-motile and measures about 3 m in lenght but may vary in size from 1 to 6 μ. The breadth is ·6 to ·7 μ. The ends are rounded and appear to bulge slightly, at other times they taper towards the ends.

STAINING PROPERTIES. The organisms stain readily with Methylene Blue sometimes uniformly but generally shewing deeply-stained granules in their interior giving them a beaded appearance: they retain the colour in Grain's method. In a field they lie irregularly scattered and do not form chains, they may be free or contained in leucocytes: (see also diagnosis)

BIOLOGICAL CHARACTERS. The organism is aërobic non-liquefying and does not form spores. The most suitable culture medium is Loeffler's blood serum - i.e. Calf's bllod serum 3 parts.

Ordinary peptone Bouillon containing 1% grape sugar, 1 part. The organism grows so much more readily on this than other mouth and throat bacilli that at the end of 24 hours colonies of Diphtheria bacilli may be seen while yet the other colonies are inconspicuous. They flourish best at ordinary temperatures of 35° C They cease growth at 20° C. The colonies appear as small rounded greyish discs the centres of which are thicker and darker than the edges as seen by transmitted light.

In Bouillon the growth and causes a turbidity which settles at the bottom of the vessel leaving the upper part clear. The medium is acid for the first three days becoming alkaline later, this acid formation is important in distinguishing the true bacillus from the Pseudo-diphtheria bacillus. On Gelatine at 22° C puncture cultures appear as a line of dots along the needle track with a rounded disc on the surface, no liquefaction occurs.

The germ will grow and flourish in milk which it does not alter in appearance.

DISTRIBUTION OF THE BACILLI. The bacilli can be found in the membrane wherever it is formed but it must be noted that Streptococci may also lead to an acute catarrhal inflammation of a mucous membrane with a semblance of false membrane. In many of the cases of non-diphtheritic sore throat those are the organisms most often found. The germs are usually found near the surface of the false membrane in the spaces between the fibrinous exudation thrown out as the result of the inflammatory reaction. In the pharynx where very abundant fibrinous exudation takes place the epithelium is raised up uniformly or in patches and because the exudation also occurs round the deeper vessels under the epithelium the false membrane in the pharynx is firmly adherent and when removed for examination purposes leaves a raw bleeding surface. In the Trachea the ciliated epithelium rapidly becomes shed and here the membrane consists chiefly of fibrin and leucocytes lying on the basement membrane and is less firmly adherent. The organisms occur in groups or clumps towards the surface or oldest parts of the membrane. The organisms have occasionally

been found in Lymphatic glands but as a rule the adenitis which occurs in the course of the illness is streptococcal in origin. As a rule it may be said that the bacilli are merely found locally at the site of infection, in the false membrane , and in the secretions of the mouth and pharynx.

Frosch (Zeitsch. f. Hygiene und Infectionskr-Bd xiii pp 49-52) was the first to note bacilli in the internal organs of patients dead of diphtheria; he found them in the Heart's blood, Liver, Spleen, Kidney, and Lymph glands in 10 out of 15 cases examined Kanthack, Kutscher and others have also found them. This distribution may be explained by their entrance into the blood stream just before death when resistance to their entrance has become abolished. In a case of a child with an unusually high temperature suffering from Diphtheria bacilli were obtained in pure culture from the blood a day before death (Welch and Schamberg Acute Contag. Dis. p.617)

Councilman Mallory and Pearce have found the bacilli in heart vegetations, the antrum, and accessory sinuses and middle ear: (loc .cit.p 618)

Virulent Diphtheria bacilli have been isolated from

the ear by Stevens and Parfitt (Journ.Path.& Bacteriol. 1897 vol iv)

Duncan Forbes (Jour.Path.& Bacteriol. 1903 vol 8.) among 40 cultures from the ears of Scarlet Fever patients found 32 bacilli morphologically indistinguishable from Diphtheria bacilli and which he regards as such.

Egerton Williams (Brit.Med. Jour. Dec.21 p.1899) found organisms which he regards as attenuated Diphtheria bacilli in the ears of four children in a fever hospital. He thinks that such may be the cause of unaccountable outbreaks in some cases and the persistence of diphtheria in other cases amongst school children.

Graham Smith examined the discharge from the ears of 10 scarlet fever cases - one had virulent Klebs Loeffler bacilli and 13 had organisms resembling Klebs Loeffler bacilli which he calls Bac.Auris and Bac. Communis. Those resembled true diphtheria organisms but differed as to rate of growth and also did not produce acid in glucose broth, out of 20 normal cases examined 13 showed Bac.Communis resembling Bacillus Diphtheriae. ... ...

ASSOCIATION WITH OTHER ORGANISMS. In the false membrane the bacilli are frequently associated with other organisims notably streptococcus pyogenes those appear to penetrate more deeply into the subjacent tissues than the Klebs Loeffler organisms

In cases of Tracheal Diphtheria Streptococci have been found associated with a false membrane (thinner and softer in character than that of the Diphtheria) at a lower level in the Trachea than the bacilli of Diphtheria. The exact significance of this association of the two varieties is doubtful, and also what part the pyogenic organisms play locally. They may possibly act as exciters of inflammation and thus, as it were, pave a way for the Loeffler bacilli - at any rate the Streptococci play an important part in the complications especially in the extensive inflammatory cervical conditions and septic poisonings sometimes met with clinically and in those cases the combined use of antistreptococcal serum and antidiptheritic serum may exert a beneficial influence.

There are other organisms morphologically resembling Diphtheria bacilli which have been described by various observers during different epidemics.

Cautley (Ref.Loc. Gov.Bd. 1894) has described an organism called by him Bac. Coryzae Segmentosus obtained from the nasal secretion of cases of influenza cold. It is non-pathogenic and shows faint acid reaction in glucose broth but grows slower than the Klebs Loeffler bacilli

Roediger (Trans.Chicago Path. Soc.Nov.9.1903) has described an organism which he calls a virulent pseudo-diphtheria bacillus: Antitoxin has no effect on cases exhibiting it. It is pathogenic to guinea pigs which are not protected by antidiphtheritic serum. Virulent diphtheria bacilli have been isolated from cases of conjunctival diphtheria by Gordon (Ref.Loc.Gov.Bd. 1901) Jessop (Trans.Ophthal Soc. United Kingdon vol xv) and others. An organism resembling the diphtheria bacillus very closely and known as the Xerosis bacillus, has been obtained from the conjunctival sac in health and disease by Uthoft (Berlin. Klin. Wochenser 1893 No.11) and others. Opinions differ as to whether the Xerosis bacillus is anon-virulent diphtheritic bacillus or a distinct species. Fraenkel (Berlin. Klin. Wock. 1896 No.12) inclines to the former opinion but most observers including Uthoft and Neisser incline to

the latter. Glucose broth remains Alkaline or becomes faintly acid, the organisms are non-pathogenic and animals cannot be protected against diphtheria bacilli by injections of cultures of this organism

POWERS OF RESISTANCE. The degree of resistive power offered by the Diph.bacilli depends largely on the moisture present. Cultures and bacilli in membrane in a moist condition offer low resistance to heat and are killed by a temperature of 60° C. in a few minutes,(Muir & Ritchie. Man. of Bacteriol p.338) But when dry cultures and bacilli in membrane possess great resistive power and will stand a temperature of 98° C for an hour. At ordinary room temperatures and in the absence of light , dry membrane may be shown to contain living virulent organisms after several months. This is an important fact in view of recurrent cases in hospital wards,,schools and private houses. Roux and Yersin of the Pasteur Institute have found that the pathogenicity of the organism is rapidly modified by sunlight and exposure to air whereas if air be excluded the diminution in toxicity brought about by light is comparatively slight -- points which emphasize the therapeutic importance

of both air and sunlight.

Fernard Arloing (Lyon. Med. Jan.19. 02) has investigated the action of Mucidine - (a solution of the mucus of red snails) upon Loeffler's bacillus - Mucidine appears from his experiments to possess a bactericidal action (after prolonged contact) but no power of combating the Toxines of Diphtheria however long the contact.

INOCULATION EFFECTS. The Klebs Loeffler Bacillus the causa causans of Clinical Diphtheria when inoculated on a mucous membrane of a guinea pig, which is a most susceptible animal - sets up local inflammatory oedema with membrane formation; when death occurs in a few days the chief post mortem change are general congestion of internal organs particularly of the supra-renal bodies where haemorrhages also occur. Broncho-pneumonia and degeneration of nerves and muscles also are found.

If death be delayed for or five days paralysis developes affecting first the extremities. Mice and rats enjoy much immunity from the toxic effects of Diphtheria.

In all animals except the cow (Klein's experiments) the bacilli remain local at the seat of inoculation.

Im the cow Klein found . . . .

the bacilli travelled per the blood stream and gave rise to a peculiar affection of the teats and udder, in the discharge of which the bacilli were demonstrable.

When the bacillus is grown on broth under certain conditions it produces in the broth certain bodies which are grouped under the name of Toxines.

THE TOXINES OF DIPHTHERIA. The precise chemical nature of the Toxines is still unknown. It is probable that the group comprises different bodies of the nature of globulins, nucleo albumins, peptones, albumoses, enzymes (Abbott Bacteriol. p.565) The subject of diphtheria Toxine has been worked out by numerous observers, Roux, Yersin Sidney Martin, Von Calcar, Ehrlich and others and is still a matter on which considerable difference of opinion exists.

Roux and Yersin (Ann. de l'Instit Pasteur ii 629: iii 273: iv 385) concluded from their experiments on animals that the chief effects produced by inoculation of cultures were due to the products of the organisms for the symptoms of poisoning occurred and led to a fatal result, even when the bacilli locally were diminishing in

numbers. Cultures also freed from bacilli by filtration proved to be highly toxic in action. The filtrate when injected into guinea pigs produced practically the same clinical effects as did the Bacilli only there was no production of false membrane. If the animals survived inoculation paralytic phenomena followed. Roux and Yersin considered the toxine to be an enzyme unstable in character and which deteriorated when exposed to light and air but which kept well in sealed tubes. The addition of an organic acid (tartaric) also destroyed its Toxicity;an alkaline medium favouring its virulencey. Those observers have also obtained Toxic bodies from the tissues of those who have died of diphtheria. A filtered watery extract from the spleen from virulent cases of the disease produced death in animals after wasting and paralysis. Sidney Martin (Ann de l'Institut Pasteur viii) has separated from the tissues, after death from virulent diphtheria, Toxic albumoses and an organic acid. He is of opinion that the bacilli produce locally a ferment which is absorbed and by its action on the proteids of the tissues gives rise to those Toxic albumoses.

The albumoses when injected into animals caused the characteristic paralytic phenomena with well marked changes in the nerves of a degenerative nature. The organic acid has a similar but milder action. Guinochet (Compt. Rend. Soc. de Biolog. 1892 p.480) has however shown that the toxine was also formed from the bacilli when grown in urine with no proteid bodies present; after growth had taken place he could not detect proteid bodies in the fluid but on account of the minute amount of Toxine present their absence could not be excluded This observer seems to prove that if the Toxine is really a proteid it may be formed synthetically in the bodies of the bacilli and not by a change in the proteid of the culture fluid brought about by their action. The subject of Toxines is further discussed by R.P. Van Calcar (Berlin. Klin.Woch. Sept.1904) Ehrlich and Arrhenius - Ehrlich supposed that the Toxines of Diphtheria consisted of two poisons, one Toxin which acted acutely killing the animal and Toxon which acted chronically in causing the palsy. Arrhenius denies the existence of Toxon, but its presence was proved by Van Calcar who employed a special dialyser. After getting

rid of the crystaloid material he put the dialysing membrane on the stretch and found that the first fluid which passed through was Toxin and when injected into an animal caused its rapid death, later Toxon passed through the membrane and upon injection was found capable only of causing Paralysis. The difference in the dialysing power being dependent on the size of the molecules. Van Calcar therefore concluded that Ehrlich's view on the plurality of the poison was correct. Ehrlich now believes the Toxin molecule to possess two atom-groups a Haptophore group by means of which it unites with certain cells of the body or with antitoxin and a Toxophore group by means of which it produces its toxic effects. When preserved for a time or under the influence of various chemical and physical elements, the Toxophore group deteriorates so that it is no longer capable of exerting toxic effects. The Haptophore group is less easily disturbed hence the combining power of the Toxin may be unaltered though it may have lost its toxic properties. In this condition it is spoken of as Toxoid or Toxone. This Toxone is still however capable of

inducing Antitoxin formation when injected into an animal, and also of neutralizing antitoxin in the same proportion as before the alteration took place.

VARIATION IN VIRULENCE of the Bacillus

The study of epidemics of diphtheria leaves no doubt that this variation may be extreme, and that during an epidemic the virulence may become more marked or vice versâ. Under certain, as yet unknown conditions, or from length of stay in the throat the virulent organism may become attenuated until it is practically non-virulent.

Two observers, Theobold Smith and E.L. Walker (28th Ann. report of the state of health of Massachusetts)1896 p.649) after careful experiments on the Toxin producing power of diphtheria bacilli concluded that all the organisms produced the same amount of Toxin and were all equally virulent. They did not meet with any non-virulent forms. Most other authorities however differ from their opinions. Roux and Yersin succeeded in attenuating the virulence of the organism by cultivating it in broth for a month at 39. 5o C. They were unable to restore its virulence if it were completely destroyed but if only partially lost it could be regained by injecting into animals the

streptococcus erysipelatosus along with the attenuated bacilli (Ency. Med. vol.3 p 11) Those observers found that by making cultures at various stages after the termination of the disease the bacilli in the mouth gradually became attenuated (Muir and Ritchie Bacteriology p.345)Spronck (Ann de l'Inst.Pasteur 1895-1898) showed that variations in toxin producing power may be due to varying quantities of muscle sugar in the broth.

Shattock (Jour. Path. & Bact. Vol.5 1898) did not succeed in raising the virulence of attenuated diphtheria organisms by cultivating them in a current of sewer air even after two months.

THE PSEUDO-DIPHTHERITIC BACILLUS.

This bacillus which is frequently to be found in the throats of patients suffering from true diphtheria has been the subject of much research and difference of opinion amongst observers as to its real nature and significance. It was first described by Loeffler in 1887 as resembling the true bacillus Diphtheriae but lacking in virulency. He regarded it as a distinct species & was corroborated in this opinion by Hoffmann whose name the organism is generally associated with. He obtained the

bacillus from the throats of healthy subjects as well as in non-diphtheritic affections. Roux and Yersin on the contrary conclude after much investigation that this pseudo bacillus is in reality a greatly attenuated Loeffler bacillus and that it bears a striking resemblance to the attenuated bacilli present in the throats of diphtheria convalescents. These observers found the pseudo-bacillus in the throats of 26 out of 59 healthy children. This is an important fact and it is not improbable that under certain circumstances, of which however we know little, they may take on a virulent phase and give rise to true Diphtheria. It is not altogether unreasonable moreover to suppose that fresh outbreaks of the disease may owe their origin to Hofmann's bacillus. Roux and Yersin were unable to render them virulent by any means but this also as we have seen they failed to do with very greatly attenuated Loeffler bacilli.

CHARACTERS OF HOFMANN'S BACILLUS. Those are generally shorter and more wedge-shaped often arranged in groups of parallel pairs, the pairs having their bases in apposition, when stained it does not present the beaded appearance of the true organism.

The colonies in cultures are more shining and white in colour and when grown on neutral broth no acid reaction is produced. - the medium becoming alkaline from the first, whereas in the case of the Loeffler organism the medium first becomes acid to be followed later by an alkaline reaction. Abbott (Bacteriology p.416) found the organism in specimens of pus derived from 30 cases of suppurating wounds. Knapp (Jour.Med. Research Vol.xii p.475, 1904) reports that the serum water media of Hiss, to which different carbohydrates are added serve to differentiate between Bac. Loeffler and Bac. Pseudo-Diphtheriticus. By inoculating the Hiss media containing Dextrine and Saccharose, Knapp claims a positive distinction may be made, for if dextrine alone be fermented the organism is Bac. Loeffler If neither dextrine nor saccharose be fermented the organism is the Pseudo-diphtheritic bacillus. Neisser's stain (see diagnosis p 114.) is also claimed by Abbott (Loc.cit.p.420) to aid differentiation.

CLINICAL SIGNIFICANCE OF THE HOFMANN BACILLUS

In discussing the spread of diphtheria by School influence reference has been made to Dr. Thomas'

paper on this subject, and a description given of the methods adopted by the London Education Committee to stamp out Diphtheria. With regard to the significance of the Pseudo-bacillus Dr.Thomas writes " All children harbouring this bacillus were at first excluded in order to err on the safe side, but it soon became evident that if this were carried out a large loss of school attendance would be necessitated. After a time such exclusion was omitted and it was found safe to ignore such organisms." This organism we are told was found in 211 out of 758 cases examined between July 17.03 and Aug.12. 04, and the true organism in 58 of the cases. By thus taking a bacteriological test as a criterion a very large diminution is effected in the number of cases requiring isolation. In this case 758 children were under suspicion of bearing infection, and it was by this bacterial examination that this number was reduced to 58 or 7.6%. By the removal of suspicion it became unnecessary to impose on 700 of the cases a needless loss of school attendance. This is very strong evidence in favour of the opinion that Hoffmann's bacillus may be disregarded as far as spreading infection is concerned. It is only right however to state that

other observers are not of the same opinion as Dr. Thomas. The experience of Dr. Davies M.O.H. Bristol (Annual Report, Health of Bristol 1903) dealing with a recent outbreak points to the view that the presence of Hofmann's bacillus amongst children who have been in direct association with cases of Clinical Diphtheria is a sign of danger as "their frequent appearance in both stages of throat diphtheria and their constant occurrence amongst contacts with diphtheria, especially in schools, lead us to attach serious importance to them when found in association with an outbreak of recognized diphtheria, and to ascribe to them the rôle of keeping alive an infection which if marked clinical cases alone occurred might readily be blotted out."

Prof. Stanley Kent who did the bacteriological work at Bristol during 1903 concludes that "evidence is accumulating to prove that the Hofmann bacillus may under certain conditions produce a disease indistinguishable from ordinary diphtheria due to the Klebs Loeffler Organism." The publication of this report led to a critical discussion on this Bacillus by Louis Cobbett and Dr. Bousfield of London. The former is entirely in agreement

with Dr. Thomas. He argues that if the Hofmann Bacillus plays the part ascribed to it by Davies it would obviously be useless to examine contacts and isolate and treat such as harbour the true Diphtheria bacillus if those carrying Hofmann were allowed to go free, and the isolation of the latter would be nearly impossible as they are by no means confined to contacts but number considerably more than half the children attending elementary schools.

Graham Smith (Journal of Hygiene April 1904) agrees with those who are of opinion that the Hofmann bacillus is entirely unrelated to the true Diphtheria bacillus and is innocuous to man. The scientific considerations on which this view is based were put to a practical test in the treatment of the Cambridge outbreak in 1900 which Graham Smith describes. Those persons whose throats contained Hofmann's bacilli only, were regarded as harmless, and were not isolated but those with Klebs Loeffler organisms were, and this measure proved sufficient to stamp out the outbreak.

From a public health standpoint it is important to consider three great types of Bacilli related to

diphtheria:

1. Virulent True Diphtheria Bacilli.

2. Non-virulent.

3. Hofmann's Pseudo Bacillus.

1. The first is obviously a source of danger and it is generally believed that this organism may be found in the throats of healthy persons who have been in contact with Diphtheria and that such persons though remaining well themselves may convey the disease to others. The Hull epidemic (pp 12.) clearly supports this. Graham Smith does not credit the view that a large number of healthy persons carry about the virulent organism. In 1511 healthy persons examined he found the true organism in but two instances. This evidence tended to show that the best means at our disposal for stamping out an epidemic is to discover contacts and isolate them till they are free from the organisms.

2. The distribution of non-virulent true diphtheria bacilli was fully investigated by Graham-Smith during the Cambridge outbreak. He found them in 1-2% of the cases examined the proportion being

the same in non-contacts as in contacts. There was no evidence to show that those non-virulent organisms ever became virulent but there were cases to show that this class of bacilli after transference from one person to another still remained non-virulent.

3. Hoffmann's bacillus is widely distributed amongst poor children especially. Graham-Smith, Cobbett and others have, as already stated, proved by practical tests during epidemics that it is apparently harmless. In the Cambridge outbreak this organism was found just as frequently among children attending a school where no diphtheria had existed for years as it did amongst the children of schools where Diphtheria has occurred. Louis Cobbett gives the frequency of the Hofmann bacillus found in healthy children as 50% Bousfield (Brit. Med. Jour.Oct.29th 04) gives the frequency at only 1%. Such a diversity of opinion leads one to suspect that various forms of pseudo-organisms are described as Hofmanns. Cobbett describes the typical form as "a rod rather wider in its middle than at the rounded ends with one narrow unstained septum in the middle. It stains with methylene

blue , and is very clear and regular in outline and shows no polar bodies. A discussion took place before the Congress of the Royal Institute of Public Health at Liverpool in 1903 on the nature of the pseudo-diphtheria (Hofmann) Bacillus and its significance in bacteriological examination for Diphtheria (Journ. State Med. Oct.1903) This discussion contains practically an Insular opinion on the subject. The Cambridge School (Graham Smith and Cobbett) stands alone in the opinion that this organism has no relation to the true Diphtheria bacillus. Bacteriologists from Bournemouth Bristol, Camberwell and Glasgow, held an opposite opinion. Hewlett of King's College summed up distinctly in favour of the view that the bacillus is a form of diphtheria bacillus though far removed in virulence. Cobbett in this paper denies any evidence to show that the Hofmann bacillus may become converted into the true diphtheria organism and vice versâ.

Hewlett and Knight (Trans.Brit.Inst. Prevent.Med. 1897) claim to have succeeded in changing by heat a true diphtheria bacillus into a pseudo bacillus which formed no acid in glucose - a method which

in the hands of Roux and Yersin (Ann.Pasteur.Inst. Vol.iv p.385) had transformed a virulent diphtheria bacillus into an acid forming pseudo-organism. These observers believe also that they succeeded in transforming a Hofmann into a true bacillus by cultivating on serum.

Richmond and Salter (Guy's Hosp. Rep. Vol.53 p 56) claim to have accomplished the same results by passing Hofmann's bacillus through small birds for which it is said to be pathogenic.

Ohlmacher (Jour.of Med. Research Vol.ii p 128) concluded after experiments that by a short sojourn in an ~~immense~~ immune animal a diphtheria bacillus may be converted into a pseudo bacillus and that the reverse may be brought about by passing the organism through a susceptible animal. His experiments only show however that a large granular diphtheria bacillus after recovery from the subcutaneous tissues of a rat became a short and uniformly staining variety, but still formed acid in glucose media. Referring to these results Corbett affirms that the Hofmann bacillus had been taken from a convalescent case of diphtheria and the possibility had never been excluded that a few diphtheria

organisms may have been stowed away with the original Hofmann.

Lesieur (Rev.in Med.News.Sept.28.'01) in agglutination experiments on the two organisms concluded that certain species of the pseudo but not others were identical with true diphtheria bacilli.

Lubowski (Zeit.F. Hygiene Bd.xxxv p 87) produced a serum by injecting the non-virulent bacillus which agglutinated both the organism used for producing the serum and also the virulent diphtheria bacillus. This serum had no agglutinative action on Hoffmann.

The evidences brought forward by Corbett in support of his views are therefore:-

1. Hofmann's bacillus produces no acid out of sugar.

2. It is non-virulent to guinea pigs even when taken from convalescents.

3. It is not agglutinated by a serum which agglutinates the Klebs Loeffler organism and the non-virulent diphtheria bacillus.

4. It does not produce Toxins.

5. The published evidences of conversion from one to the other are insufficient to be relied upon

6. Hofmann's bacillus is widely distributed and occurs no oftener in contacts than in persons from healthy districts.

Dr. Heaven M.O.H. Bristol brings forward evidence in favour of the view that under certain conditions (which may not be present in laboratory experiments) the Hofmann bacillus may be converted into forms morphologically accepted as diphtheria bacilli and give rise to illness and inferentially to Diphtheria. From his experience of an outbreak in Avonmouth (Pub.Health June 1903) he shows that until contacts with Hofmann were isolated the disease was not stamped out. He further records cases of 25 children, yielding Hoffmann only, who were treated in a Diphtheria Ward, none of whom contracted the true disease presumably being in some way rendered immune by the Hofmann organism. He also gives cases only showing Hofmann bacteriologically who developed symptoms akin to post-diphtheritic paralysis and at least one such died of cardiac failure. Yet again (Pub. Health Vol.xv p 529) Heaven gives one instance in which a culture from a case, which in many previous cultures never showed any organism save Hofmann, was found by Klein to

kill guinea pigs in the same manner as Diphtheria does. He goes on to prove that in another set of cases Hofmann bacilli were obtained on the first examination but that later examination revealed true Klebs Loeffler bacilli, he is of opinion therefore that transition forms between the two are numerous. It is just possible of course that in reality the true organisms were present in the first instance but escaped detection.

Buchannan of Glasgow, Bousfield (Camberwell) and Prof. Stanley Kent (Bristol) all incline to the opinions of Dr. Heaven and that the Hofmann bacillus may act as a "Materies morbi" for the spread of the disease and the tendency is towards Hofmann forms during convalescence from diphtheria. Hewlett of Kings assumes degrees of non-virulence as well as of virulence. The non-virulent true Diphtheria organism he would classify as not far removed from virulence and the Hofmann as being far removed in virulence. He thinks this would account for the difficulties experienced in converting Hofmann's bacillus into a virulent specimen.

After due consideration of the opposite opinions expressed by these two schools, on the exact relationship and significance of Hofmann's bacillus it is

evident the matter cannot be considered as finally decided on any definite grounds. Very weighty evidence has been brought to bear in favour of the close relationship to Klebs Loeffler organisms by eminent authorities in this country France and America. Still one must admit that opinion in favour of the opposite view has accumulated and is steadily gaining ground and moreover has stood the test in practical work in more than one epidemic. During my residency at Lincoln Hospital an epidemic clinically resembling diphtheria occurred in the children's ward. Seven children and one nurse were attacked, one child died suddenly of cardiac failure. A swabbing from the throat of one of the cases sent to the Clin. Research Assoc. London for examination was reported as "Pseud. bacilli alone present." The cases were isolated and treated as diphtheria. One child developed paralysis of the legs and the nurse just escaped tracheotomy.

Clinically it is possible to draw sound and useful Corollaries from what has been actually established. When suspicious throat cases have been examined by a competent bacteriologist who reports "true Bacilli are present." the course indicated is obviously to isolate the patient, established throat disinfection, and dose with antitoxin.

Repeated examinations of discharges should then be made till assured that the bacilli have disappeared If such isolation be taking an unduly long time and the true bacilli are still reported present one may then ascertain by inoculations on guinea pigs if the organism be still virulent. If this be so continued isolation must be insisted on. if they are not virulent to animals it is still desirable to get rid of them but the danger to others is much less. Should the report read "Hofmann bacilli alone present" and the throat symptoms be mild in character one might be justified in risking infection to others and have the satisfaction of knowing that a considerable weight of scientific opinion, though by no means the whole of it, was on one's side. If the throat symptoms were severe, temporary isolation would certainly be advantageous combined with local and serum treatment. Moreover one would be more suspicious of the Hofmann if occurring in the throats of contacts than if it occurred in healthy children. Special emphasis ought to be made on the necessity of repeated careful examinations of the nose secretions as it has been found that the nose may give positive bacteriological proof of the existence

of both the Klebs Loeffler bacillus and the pseudo diphtheric forms. Considerable danger to the public health arises from those latent cases of nasal infection, the only manifestation of which may be a "stuffy nasal condition" with slight catarrh. It is remarkable how long diphtheria bacilli will persist in the nasal passages. The study of 220 fatal cases of diphtheria by Councilman, Mallory and Pearce (Philadel. Med. Jour.May 4.03) and the investigations into the bacteriology of nasal sinusitis by Howard and Ingersoll (Aner.Jour. Med. Science May 1898) Conclusively prove that diphtheria bacilli, like Friedländers bacillus, the bacillus of Influenza and various pathogenic organisms may reach and persist in the accessory air sinuses, Cases of nasal accessory sinus disease may discharge for years, and thus may be explained a persistent recurrence of diphtheria bacilli sometimes observed in nasal discharges dispite careful antiseptic nasal irrigation. During the past few years diphtheria has invaded the Children's Hospital at Nottingham. As part of an endeavour to prevent re-invasion the throats and noses of all cases admitted were examined for the diphtheria bacillus. The swabs were inoculated within a few hours on fresh blood serum and ... ...

incubated for 18 hours. A film from each tube was stained with Loeffler's Methylene Blue and in the majority of cases a 2nd film was stained by Neisser's method. In 113 cases a good growth was obtained from the nose and throat the results being as follows:-

DIPHTHERIA BACILLI PRESENT		PSEUDO DIPHTHERIA BACILLI PRESENT	
In nose and throat	2	In nose and throat	15
In nose and ear	1	In nose only	41
In nose only	1	In throat only	21
In throat only	2		
	6		77

Both baccilli absent 30.

Dr Heaven (B.Med.Jour. Sept. 16.05) from the culture examinations of two schools found.

Nose alone affected	17	with Diphtheria bacilli
" " "	93	with Hofmann
Throat " "	1	with Diphtheria Bacillus
" " "	5	with Hofmann
Both throat & Nose	5	with Diphtheria bacilli
" " "	8	with Hofmann.

DIAGNOSIS OF DIPHTHERIA. As Diphtheria is a communicable disease with a decided predilection for young children it is of the utmost importance that an early diagnosis be made, not only with regard to Prevention but also because early treatment is the key-note to success. To the general practitioner few cases are so worrying as dubious throat cases and this especially in the absence of a prevailing epidemic. Mistakes in diagnosis are alike serious to the individual, the community and to the reputation of the practitioner in attendance. There is no throat disease which may be so varied in its early manifestations. A copious exudate leaves no doubt as to the nature of the infection and fortunately this exudate usually shows itself at an early stage, but unfortunately many cases make no complaint of throat trouble as an early manifestation. A golden rule therefore is to examine the throat of all feverish children. In private practice one finds cases of this disease with enlarged cervical glands mistaken by the

patients' friends for Mumps and under this delusion are treated as such with pernicious effect both on the patient and those who may come in contact with the case. Where there has been recent exposure to infection the mildest form of "sore throat" must be regarded with suspicion and a bacteriological examination at once instituted; a muco-purulent nasal discharge with crusts about the nares will add liklihood to the assumption of a case being diphtheria. The prodromata are not sufficiently characteristic to be relied upon to aid an opinion. The characters of the exudate will give great assistance- its situation, especially on the uvula is, by some, regarded as pathognomonic, when forcibly removed the exudate leaves a raw bleeding surface, enlarged cervical glands are rarely absent.

FOLLICULAR TONSILLITIS is the throat affection most apt to be confounded with Diphtheria. The prodromata are practically indentical- the initial rise in temperature may be greater than in mild Diphtheria. The diagnosis is especially difficult where diphtheria begins in and around the tonsillar crypts. The exudate in Tonsillitis is softer and does not spread to adjacent parts. Albuminuria is rare. The exudate in simple cases is

easily rubbed away by a swab and no bleeding results. The patches occasionally formed in Thrush may give some difficulty but as a rule are easily recognised. Their occurrence in marasmic children and in adults suffering from wasting diseases along with the whiter colour and unmistakable microscopic appearances and absence of general symptoms will usually clear up the doubt.

SCARLET FEVER. In the absence of the rash a differential diagnosis may be difficult. The febrile symptoms are more pronounced, the pulse is more rapid and delirium, rare in diphtheria, is frequently present in Scarlatina. Vomiting would increase the presumption of the case being non-diphtheritic, as would a very red hue of the fauces.

CATARRHAL OR SPASMODIC CROUP resembles Laryngeal diphtheria in many respects. In the latter the symptoms are progressive in character and not, as in spasmodic croup, apt to be worse at night than in the day-time. The hoarseness of Diphtheritic laryngitis gradually increases till the voice becomes a whisper. In false croup the voice is

rarely lost altogether or even reduced to a whisper An emetic will give relief in spasmodic cases, but will not succeed in greatly altering the dyspnoea of true croup. The respiratory stridor in false croup may reach a height of noisiness rarely seen in true diphtheritic croup.

Paralysis of the abductor muscles of the vocal cords in an adult, of sudden onset may closely similate laryngeal diphtheria (Gibson's Med. Vol i p.213) and may even end fatally.

BACTERIOLOGICAL DIAGNOSIS

In all but the most evident cases this method should be employed to solve the difficulty. Positive results are conclusive but negative results, in clinically suspicious cases, must not be relied on especially ONE negative result. The presence or absence of the Klebs Loeffler bacilli may be demonstrated in a few minutes by examination of smears taken from the throat and stained with Loeffler's Methylene Blue.

This stain is made up of :

Concentrated alcoholic solution methylene blue...30 C,C.

Caustic Potash (1 in 10,000) 100 C.C.

This is a rapid and useful method which in many instances will clinch a diagnosis, but again in

certain cases the value of such examination is only a relative one because the organisms may be much less typical in appearance than those of culture films and the risk of contamination is necessarily great. There are other organisms in the mouth cavity, particularly in the mouths of patients suffering from decayed teeth, the morphological characters of which are similar to, and apt to be mistaken for the Diphtheria organism if subjected to the usual method of examination(Abbott. Princ. of Bact. 5th Ed. 1899 p.351) In the presence of clinical evidences however such smears will confirm or negative a diagnosis in many cases.

H.A. Higley (Medical Record April 1st 1905) gives the following method for making a rapid (fifteen minutes) and sure diagnosis of films from the throat. The exudate is obtained in the usual way and fixed in a flame. The following are the stains:-

No.1 Five drops Kühnes carbolic methylene blue in 7 c.c.m. tap water, applied for five seconds Wash with tap water and dry with filter paper then apply.

No 2 Ten drops carbolo-fuchsin in 7 c.c.m. tap water for one minute. Wash, dry, and mount

in balsam:

The Diphtheria bacilli appear as dark red or violet rods irregularly stained, often containing polar dots. " The unevenness of their contour and mode of division are clearly brought out and these characteristics afford the essential differential points, for other organisms take varying tints and may appear the same colour as the diphtheria bacilli so that in colour alone no differentiation is possible"

In obtaining material from the throat in a suspected case, care must be taken to do so before the use of antiseptics as gargles or paints. A sterile swab on a short stout wire is rubbed over the exudate where this is present, or on the tonsils and pharyngeal wall if absent, care being meanwhile taken to keep the tongue out of the way by a spatula. In addition to smear films, cultures should be made from the swabbing thus obtained and the colonies examined microscopically. By these means a certain opinion will usually be formed or recourse will be made to Inoculation of animals. As already stated Blood Serum is the best medium. Incubated at 37° C. for 12-14 hours colonies will be visible and ready for

examination (see Bacteriology) A small colony is then mixed with distilled water, films prepared and fixed by heat after drying in air. If Loefflers methylene blue be used as a stain, it may be allowed to act for 10 minutes after which the films are washed, dried, and mounted in balsam. Examination should be made with a 1/12 in. oil immersion lens.

Abbott (loc.cit) recommends Neisser's stain as offering special advantages in overcoming difficulties experienced in differentiating the Loeffler bacillus from other organisms present. Neisser's stain is:-

Methylene Blue (Grübler)	1 part
Alcohol (96 %)	20 parts
Distilled Water	950 parts
Glacial Acetic Acid	50 parts

Films are stained for 3-4 seconds, rinsed in water and counter-stained for 3-4 seconds in:-

Vesuvian (Bismark Brown)	1 part	)
Boiling distilled water	500 parts	) filtered

After rinsing again dry the films and mount in balsam.

When so stained the Bacilli appear as faintly stained brown rods in which three or four bright

blue granules (Babes - Ernst bodies) are to be seen. Those are situated at one or both poles and if a third be present it is in the centre of the rod. Those bodies have a greater diameter than the rod and cause a bulging in the contour of the bacillus. In the majority of cases it seems safe to regard all bacilli which do not stain in this manner as distinct from the true Bacillus Diphtheriae. J. Wicliffe Peck (Lancet Jan.10. 1903) gives another differential stain for the Klebs Loeffler bacillus. He uses Loeffler's methylene blue for 3 ~ 4 seconds and counter-stains with vesuvian (o.2.% aequeous solution) for 30 seconds. He thinks this more advantageous than the Neisser's acetic acid stain. He adds "the common mouth organisms do not stain in the 3 seconds required, and neither the bacillus Hofmann nor the bacillus Segmentosis stain by this method"

One cannot estimate the toxicity of a specimen from the morphological character, nor is one justified in concluding that the bacillus is not a true diphtheria bacillus because it is devoid of

virulence, though the intensity of its Toxin will obviously have an important bearing on the Clinical History of the case in which the organism is found. Such non-virulent bacteria must moreover be distinguished from the pseudo-diphtheritic organism of Hofmann. These may morphologically resemble the Klebs Loeffler bacillus, but differ under culture and inoculation test as referred to under Bacteriology, and such tests may in certain cases be necessary as a means of differentiation.

C H A P T E R. VIII.

PROGNOSIS OF DIPHTHERIA.

In considering the outlook in a case of Diphtheria it is necessary to take account of the age, sex, locality of the disease, type of epidemic prevailing, Social status of the patient, temperature, pulse, complications, and especially the duration of the illness before treatment is begun:

1. AGE AND SEX. Statistics show that the greatest fatality occurs in children under 5 years of age, and that most deaths occur in males without obvious reason. For table of mortality according to age see p.p. 8

The following table shows the relative mortality according to sex in 1000 cases observed by Lennox Browne (Diph.& its Associates)

	Admitted	Died	Mortality per cent.
Males	533	162	30.39
Females.....	467	122	25.91

2. LOCALITY OF THE DISEASE.

Laryngeal diphtheria is a most fatal form: Severe nasal involvement along with marked faucial trouble

is to be viewed with grave apprehension as toxaemia is apt to be severe. In general terms the danger is increasingly grave in proportion to the extent of surface involved and the copiousness of the exudation. In Lennox Browne's 1000 cases the mortality according to site of the exudate was as follows:

	Cases	Deaths	Mortality per cent
Fauces alone	666	81	12.16
Lyrangeal cases) alone)	4	1	25.00
Nares alone	2	1	50.00
Fauces and) Larynx)	112	51	45.53
Fauces and) Nares)	165	106	64.24
Fauces Larynx) and Nares	49	30	61.22
Buccal cavity) and lips)	6	2	33.33
Membrane involv-) ing hard palate)	12	11	91.66

It will be noticed in studying this table the high rate of mortality resulting from involvement of the nares and fauces. In a case where the nasal cavities are plugged with exudate and which show marked faucial exudate the outlook is far from encouraging. Epistaxis isa source of danger in itself. Systemic poisoning however, through the lymphatics in the mucous membrane and submucous tissues is the..... ....

greatest danger, death may result from asthema or heart failure. Paralysis is likely also to be developed during convalescence. Meningitis following nasal involvement is quoted by Lennox Browne (loc.cit.)

3. TYPE OF EPIDEMIC PREVALENT Some epidemics are mild in character and others associated with a high death rate.

4. THE SOCIAL STATUS. affects the prognosis in curious ways. Diphtheria breaking out in an institution for children is apt to be severe. Amongst 7 cases which occurred in the children's ward at Lincoln Hospital during my residency, two proved fatal, one was followed by severe paralysis in both legs, and the others varied in severity. When the disease attacks members of the upper classes it runs a severe course probably because it finds a more receptive soil in delicately nurtured patients than in those accustomed to a rougher mode of life. On the contrary recovery from the sequelae is more expeditious in the well-to-do for reasons which are obvious.

In severe epidemics bad sanitation, lack of adequate ventilation and fresh air in the sick room

tend by lowering the resistive powers to contribute towards a fatal result.

5.TEMPERATURE. As a prognostic guide in Diphtheria the temperature is not of much value: my experience of the disease is that it is not one associated with great fever. The persistence of a high temperature after the first few days of illness generally points to a complication, the most likely of which is a catarrhal pneumonia. A falling temperature (sub-normal) on the contrary with signs of increasing Toxaemia is to be feared as death may occur from Asthenia. A high temperature again in septic cases with much glandular affection is correspond-ingly grave.

6. PULSE So long as the pulse remains regular, of good volume and does not exceed 115-120 per minute in a child or fall below 50 in an adult all is probably going on well. A pulse of 140 or 160 in a child prior to Tracheotomy in laryngeal cases is frequently observed and yet is not necessarily of fatal significance. The pulse volume and rapidity largely depend on the toxic absorption affecting the cardiac nerves and leading possibly to myocardial changes. When cardiac action becomes

slow there is danger of clot formation in the interior of the heart or large vessels connected therewith. Cardio-pulmonary seizures are alarmingly sudden in onset and very grave in significance. Vomiting is generally an initial symptom to be followed by signs of asphyxia and heart failure - dyspnoea, cyanotic pallor, and great restlessness with coldness of the extremities. Such cases seldom recover.

7 COMPLICATIONS. A highly albuminous urine when associated with casts warrants a grave prognosis. Suppression of urine with perhaps uraemia spells death as a rule. Slight albuminuria is not of much importance. Broncho-pneumonia superadded to laryngeal diphtheria adds an increased danger to an already severe type of disease.

The prognosis should be greatly qualified when diphtheria is associated with other diseases such as Scarlet Fever and Measles. In 1900 measles cases of a malignant type occurring in the Diphtheria Wards of the Municipal Hospitals Philadelphia - the mortality was 50% (Welch and Schamberg Ac Contag. diseases p.686)

Paralysis adds danger according to which part is affected. Palatal paralysis is not serious. Recovery is the rule in average cases of general paresis. When deglution is paralysed there is some danger of starvation unless nasal feeding be practicable. Septic pneumonia may supervene through food entering the larynx. Cardiac paralysis gives the worst prognosis. It may supervene so suddenly as to end the scene in a few minutes. It is liable to occur early or late in the disease. Early Cardiac paralysis is the most serious form. In this condition vomiting, restlessness, inequality of pulses, weakness of the cardiac first sound, subsequently a gallop-rhythm (even when temporary remissions take place) occurring during the first fortnight are of very fatal omen. M. Marfan (Bull.de la Soc. Med. des Hôp. de Paris 1902) draws attention to two signs of particularly grave import in cardiac cases. The first is a progressive enlargment of the liver due to congestion from cardiac failure and in part to albuminous degeneration produced by the toxines. The second which Marfan calls "le signe des genoux" consists in the appearance of a

scarlatiniform eruption on the knees sometimes also on the elbows. This occurs independently of serum injections and was described in pre-antitoxin times. Respiratory paralysis especially if associated with palsy of the diaphragm is a most serious complication with the attendant risks of Asphyxia and Pneumonia. In Conjunctival Diphtheria there is risk of destruction of the globe. Middle ear trouble does not usually lead to permanent impairment of hearing.

Of special symptoms which may arise during an attack of Diphtheria the following must be regarded as ominous - frequent vomiting or retching, haemorrhages from mucous membranes and into the skin and convulsions. The general appearance of the patient is a valuable guide as to the course of a case. A fatal result may be looked for if the face in a severe case becomes pale & sallow with a smooth shining appearance of the skin, if the neck in addition be oedematous and if the whole aspect betokens a condition of apathy. Towards the end of such a case a livid hue is added to the countenance Petechiae may be present in the skin from

the severity of the blood poisoning and toxaemia

8. THE DURATION OF THE ILLNESS BEFORE SERUM TREATMENT IS UNDERTAKEN is a most important element in giving a hopeful outlook or otherwise. The Bulletin issued by the Health Department of Chicago Feb.13th 1904 contains statistics of 7435 cases as follows:

Day on which Antitoxin was injected	Cases	Deaths	Mortality per cent
First day	586	2	.34
Second day	1913	28	1.46
Third day	2624	85	3.24
Fourth day	1374	148	10. 8
Later than 4th day	936	216	23. 1
Total	7433	479	6.44

This table clearly shows that with serum treatment on the first day of illness the mortality is practically nil, but if delayed till the 4th day may reach 10.8 %, which is a fairly high rate of mortality in antitoxin treatment.

C H A P T E R. IX.

THE TREATMENT OF DIPHTHERIA.

In dealing with the treatment of diphtheria it is necessary and important to recognise that one has not only to face well marked cases of the malady but also aberrant or atypical forms in which nearly all of the clinical signs and manifestations of typical diphtheria are absent. In the interests of Public Health it is of great moment that such cases be recognised in order that appropriate treatment may be speedily adopted. One fact which must be grasped above all others is that directly there is the least suspicion of a case being diphtheritic in nature, serum treatment must be instituted without delay and no time ought to be lost in waiting for a bacteriological report to confirm or negative such suspicion for the administration of antidiphtheritic serum with due precautions is unattended with risk. The practitioner called to a case of doubtful sore throat will have done the best by his patient if he inject an ordinary dose of serum say 2000 units and thereafter obtain a swabbing from the throat for examination, No harm has been done to the patient and if the case prove to be true Diphtheria an incalculable advantage is gained by this means -

For present-day knowledge shows beyond a doubt, that if antitoxin treatment is undertaken on the first day of the illness, Diphtheria should be practically a non-fatal disease. Moreover it has been shown that the administration of the antidiphtheritic serum is beneficial in other forms of sore throat particularly those of a Scarlatinoform nature (Basil Rhodes Brit.Med. Journal Feb.17, 1906)

SECTION I

SERUM TREATMENT has for its object the combating of the Toxines which are formed locally by the Klebs-Loeffler bacilli, and which circulate in the body and are responsible for the occurrence of the various complications of the disease - the destruction of Red blood cells with accompanying anaemia, the paresis, the nerve degenerations, fatty cardiac changes etc. Accepting Ehrlich's Seittenkette or side chain theory of Immunity we desire to prevent the toxines entering into combination with nerve and other cells because after such combination has taken place antitoxin has but little chance of neutralizing the effects of such union but even in late cases serum is valuable in that it prevents further union between cells and toxines.

Ehrlich's theory was proposed in 1897 (Klin.Jahrbuch 1897 Bd. vi Heft 2 s. 309) and is the most recent interpretation of the phenomena of acquired immunity. Ehrlich conceives the individual cell to be a complex molecule comprising a central nucleus to which are attached by side chains its secondary atom groups. Injury to one or more of these physiologically essential atom-groups results in disturbance of the cell-equilibrium and consequent effort on the part of the surrounding atom-groups at compensatory repair by an excitation to bioplastic activity. This liberation of energy generates more plastic material than is actually required to repair the injury and the excess of this material finds its way into the blood and is regarded by Ehrlich as the real antitoxic substance This substance combines directly with the intoxicant to form physiologically inactive toxin thereby rendering the animal immune. (Ehrlich "Zur Kenntniss der Antitoxin-wirkung. Fortsch der Medicin 1897 Bd. XV No.2) Ehrlich's theory assumes that antitoxin has a stronger affinity for the Toxines than the Toxines have for the body cells and so the antitoxin acts by combining with the toxin preventing the latter from doing harm. The earlier the administration therefore the greater the value.

Delay means damage and unfortunately such a time may be reached that the patient has absorbed a fatal dose of Toxin and is beyond the reach of cure even if we are successful in preventing any further combination. Serum may be considered therefore as Preventative, by anticipating the combination between cells and toxines and Curative in that it allows the phagocytes , which would otherwise be paralysed by the toxines, free play to cope with the bacilli themselves. Personally I have always used the serum supplied by Burroughs, Wellcome & Co., and find it efficient and free from rash producing properties. The quantity injected necessarily varies with the severity of the case and also the day of the disease. It is unfortunate in general practice that patients who have a great dread of the word Diphtheria are so ignorant and prejudiced against consulting a Doctor for slight sore throats and so it is not unfrequently the 3rd or 4th day before one sees the case for the first time.
An initial dose of 2000 units followed in 6 hours by a similar dose may suffice in mild cases. The precise dose required in any individual case must of necessity be empirical as we cannot gauge the amount

of Toxin present in the system. One is guided by the appearance of the patient, the amount of membrane and its tendency to separation, by the pulse and temperature. The condition and not the age of the patient must be the main guide, pallor indicating toxaemia and a pulse of say 160 per minute with a temperature of 100° F. indicating a probable toxic myocarditis and thus demanding increased dosage. The temperature in Diphtheria is not in my experience a very high one, a typical effect of Antitoxin is to cause a fall in 12-24 hours. The glandular affection also is a good guide the enlargement being an attempt on the part of the system to check the spread of the Toxines. The further away from the seat of the lesion one finds enlarged glands the more serious is the case to be considered and thus demands large doses of antitoxin. A copious faucial exudate and also severe laryngeal cases indicate vigorous serum administration.

At a meeting of the Section of Pediatrics of the New York Academy of Medicini (Med.Rec.Nov.26.04) A discussion was invited on the relative merits of large and small doses of serum founded on

accurate statistics of the Willard Parker Hospital a summary of which is appended. The results show a mortality of about 21 % with small doses and 14 % with large doses.

Total cases treated in July 1903 134	Pgaryngeal & Tonsil cases 107	Deaths 18% Recoveries 82.3%	Average dose Antitoxin 1500 units.
	Tube cases 34	Deaths 17% Recoveries 50%	
Total cases treated in July 1904 134	Pharyngeal & Tonsil cases 100	Deaths 11% Recoveries 89%	Average dose Antitoxin 2500 units " "
	Tube cases 34	Deaths 20% Recoveries 73.5%	
Total cases treated in August 1904 121	Pharyngeal & Tonsil cases 97	Deaths 6% Recoveries 93.5%	Average dose Antitoxin 5000 units
	Tube Cases 24	Deaths 10% Recoveries 58%	
Total cases treated in Sept.1904 137.	Pharyngeal & Tonsil cases 105	Deaths 7% Recoveries 93.3%	Average dose Antitoxin 5000 to 10,000 units
	Tube cases 32	Deaths 11% Recoveries 65.6%	

It is the practice in the Hospitals of the Metropolitan Asylums Board to administer very large doses of antitoxin - 12,000 units or more.
My own experience of diphtheria has led me to favour repeated small doses 1500 - 2000 units provided one gets the case early in the disease. This is a point of importance in private practice because if it be insisted on that very large doses are essential I fear fewer general practitioners than at present will resort to serum treatment in any but the better classes on account of the great expense incurred to the patients. Personally I enter a plea that authroities on this subject impress on the profession the undoubted value of moderate doses of antitoxin. Gasparini (Gazz. degli. Osped. Feb. 18. 06) publishes his results based on 150 cases of Diphtheria in which the mortality was 7.33% and no case had more than 6,000 units of antitoxin.
Park (Loumis Thomson Amer. Sys. Pract. Med. Art. Diph.) says "the size of the dose should be ~~increased~~ measured chiefly by the extent and intensity of the disorder also, but to a less degree by the size of the patient and the duration of the illness" For

young children with but moderate lesions on the tonsils or palate a single dose of 1000-1500 units will suffice. For older children and adults 1000-2000 units should be given. In children seriously ill or showing toxic effects or in whom the larynx is involved a dose of 1500-3000 is necessary"

METHOD OF ADMINISTRATION.

Hypodermic injection is the usual method employed in administrating the serum. In children I find it easier to inject the serum subcutaneously between the shoulder blades there being less risk of the child moving and breaking the needle as has happened in my knowledge when the abdominal wall was the site chosen. Naturally all antiseptic precautions are observed with regard to both syringe and skin. In desperate cases intravenous injection should be considered as the effect is more quickly attained.

Cairns (Lancet Dec.12. 02) advises intravenous injections in malignant cases, in profoundly toxaemic cases and when the lungs are much involved. He recommends injection of 20,000-25,000 units at once and repeated in 24 hours if no improvement takes place. His observations are

on 20 cases treated at the Belvidere Hospital, Glasgow. In 6 out of the 7 cases related at length however tracheotomy had to be performed for accompanying asphyxia and no doubt this went far to produce the marked alleviation of symptoms and so it is difficult to gauge the exact benefit of the intravenous injections, still in such cases as he describes where the effect is urgently required this method would doubtless prove of some value. L. Cruveilheir (Ann.de l'Instit.Pasteur.Jan.1904) made observations on the utility of injections at various sites. He concludes that "Intracerebral injections are more efficacious than the subcutaneous but intravenous injection is the method of choice and a most valuable therapeutic measure. His experiments were done on guinea-pigs in which also he found massive doses more efficacious than mean doses and that the dose should be repeated in all serious cases. Subcutaneous injection of 1/10 c.c.m of serum was successfully used 10 hours after inoculation with a standard lethal dose of culture, the period was extended to 12 hours by the use of massive doses. Intracerebral injection lengthened the period from 12 to 14hours but intravenous

injection was efficacious up to 16 hours. Similar results were obtained in animals inoculated with toxin instead of cultures.

Of administration of Antitoxic serum orally I have no experience but one cannot but fear that the constituents would be altered by the various chemical contents of the stomach. Hewitt has shown by experiments on animals that this is not an efficacious method of administration. On the other hand Dr. Pilcher of Sheffield reports a series of cases (Brit.Med.Jour.Feb.17. 1906) tending to prove that in mild cases this method may be useful. In severe laryngeal cases however Pilcher seems to have been obliged to resort to hypodermic injections especially where a rapid result was desirable. The serum should be given on an empty stomach and no vomiting should be present. park Davies & Co have a low potency serum specially prepared for oral administration. Its effect is neither anti-bacterial nor antitoxic, but rather it is given to increase tissue resistence while given along with subcutaneous injections of antitoxic serum.

Montgomery Paton (New Serum Therapy 1906 p.71) quotes cases of Diphtheria treated by this dual method

which have shown rapid improvement and no paralytic phenomena. The dose is ℥i every three hours. Paton is of opinion that by its regular and continued use the tone of the tissues may be so raised as to obviate many of the complications attending the disease. He has further shown that the oral use of Normal plasma of the horse in ℥i doses t.id. will in cases of non-microbic illnesses with deficient bodily function through lack of nutrition i.e. a debilitated nursing woman, produce a restoration of function. Paton experimented on dogs to ascertain if the Oral use of Anti-diphtheritic serum would save them from a lethal dose of Toxin. Two dogs received intravenously 2 C.C. of the same Toxin. One dog received orally two ounces of serum during the next two days and made a good recovery. The control died in 4½ days. Paton conducted a series of six such experiments which gave varied results and are insufficient upon which to form an accurate opinion, but his conclusions are worthy of note and warrant a trial of oral administration in addition to hypodermic use of serum, the one with a view of raising Tissue Tone and producing as it were an unsuitable soil, and the other to neutralise the

Toxines in the tissues. A result which, if attained, forms an ideal combination of therapeutics in any microbic infection.

COMPLICATIONS ATTENDING SERUM INJECTIONS.

Various objections have been raised at times to the employment of serum because of certain unpleasant complications attending its use, but at the present day there are few medical men who do not believe in its efficacy. Among sequelae the occurrence of local abscess at the site of inoculation must be remembered care in antiseptic preparations should obviate this trouble and also one should avoid using serum which does not look clear in the phial. Another important point is to see that no air is injected with the serum. It is just possible that the occurrence of mixed infection, diphtheria plus streptococci, may determine suppuration. Rashes occur in 30-45% of cases treated by serum (Ency.Med. Vol.3 p.17) usually taking the form of Erythemata but all erythemata following the use of serum are not due to the anti-toxin for certain cases of Diphtheria not treated with serum sometimes show during the 3rd week of the illness Erythema of various types usually scarlatinoform. The true antitoxin rash may

occur as early as the first day but its usual appearance is delayed till about 10-12 days after injection, it may occur as late as the 3rd week. The rash may be regarded as a conservative attempt on the part of the skin to rid the system of a foreign material in the blood. Berg.(New York Med. Record. June 18th 1898 pp865-873) used serum filtered through a Chamberland filter and concluded that the filtered antitoxin is less liable to give rise to rashes after injection. Rumno (Quoted by Berg.loc.cit.) believes that the toxic effects are due to the action of special toxalbumins.

Schmid.(Ibid) is of opinion that the effects depend upon the action of soluble fibrin ferment of one blood serum upon the second animal. Frequently the rash closely resembles Scarlet Fever, but it generally occurs first at the seat of injection, sickness is absent and the temperature but slightly raised. The rash persists for a few hours or several days and is accompanied by little constitutional disturbance beyond malaise. An injection of the fauces may occur at the same time further completing the simile to Scarlet Fever, and there is just a danger of such cases being sent to an

infectious hospital as such, and the patient is liable to be attacked with Scarlatina in consequence. Powdery des-quamation is also an occasional result of the antitoxin rash, the diagnosis in these cases being most puzzling.

Netter (Com.Société de Biologie 1906) made a communication on the prevention of antitoxin rashes by the use of calcium chloride. Each child received on the day of injection and the two following days 1 grain calcium chloride. From Jan.15.1905 to Dec.31. 05 every alternate child admitted into the Diphtheria wards of the Trousseau Hospital was thus treated. 258 in all. Of those who did not receive the calcium 15.53% showed rashes while only 2.38% of those receiving calcium were thus affected. The calcium has no detrimental effect on the efficacy of the serum. The dose of calcium chloride should be in proportion to the quantity of serum given and the number of injections.

Arthritis and Peri-arthritis occur after serum injection in about 6% of the cases (Ency.Med.Vol iii p.18) There is no swelling of the joints as a rule but merely pain. The shoulders, hips, elbows and knees are the joints usually complained of, and the

affection generally occurs along with the rashes described, the pains last about four days. Pericarditis and Endocarditis do not occur. The fascia and tendons about the joints may be more tender than the actual joints. Concentrated sera seem less liable to give unpleasant sequelae than those in which a large volume is injected. Rigors have been known to follow serum injection, but I have never seen collapse or prostration follow its use.

NIFONG (Med. Review May 7. 1898) gave a boy of 15 years, of slight build and with feeble circulation, 1500 units. Death followed in 35 minutes preceded by pallor, numbness of the extremities, cyanosis and vomiting.. Transient albuminuria has also been recorded but suppression of urine never occurs.

. Marsden (B. Med. Jour. 1899 p.197) believes the early use of serum lessens the liability to albuminuria and that when it occurs late in diphtheria it may be due to the use of antitoxin.. On the whole the complications attending this valuable therapeutic remedy are not of great practical importance.

Winter of New York (Med.Record. June 20. 1896)

believes that pneumonia in diphtheria has become more frequent since the employment of serum treatment He regards it as septic in character. Kucharzewski (Arch. Internat.de Pharmacodynam et de Thérapie 1904 vol 12 p.117) has tested the effect of injections of Antidiphtheritic serum on the blood of healthy animals (rabbits) The serum produces a slight and transient decrease in the number of red blood corpuscles and in the amount of Haemoglobin. the specific gravity showed no constant change. Small doses of serum produced no leucocyte re-action larger doses caused a leucocytosis lasting several days. The bodily weight of the animals was slightly diminished. His conclusion was that the serum had no prejudicial effect on the animal economy beyond that which the normal serum free from antitoxic substances possessed. Ewing (New York Med. Jour. Aug.17.1905) studied the effects of Antitoxin on the number and nature of Leucocytes. While Leucocytosis begins soon after the invasion of Diphtheria and increases mainly as regards myelocytes up to the climax of the disease and steadily decreases during convalescence - remaining high

only in bad and fatal cases. Antitoxin causes, according to Ewing, a reduction in the leucocytes within 30 minutes of the injection. This affects the uninuclear variety while the proportion of well stained multinuclear leucocytes is increased. In favourable cases the leucocytosis never again reaches its original height after injection, in severe cases it is followed by more leucocytosis in a few hours The multinuclear cells found in the blood in favourable cases after serum treatment show an increased affinity for Gentian Violet. The non-occurrence of this change, Ewing says, is a very unfavourable prognostic sign.

The value of Antitoxin in treating cases of diphtheria is placed by statistics beyond the region of a doubt. In 1897 Rauchfüss (Quoted by Bayeux La diphtherie, Paris 1899) presented to the International Medical Congress at Moscow the most extensive statistics that have yet been collected on the subject of Serum therapy in Diphtheria. They give results of enquiry throughout the Russian Empire. The figures include 44631 cases of positive diphtheria and are as follows:-

DIPHTHERIA TREATED WITHOUT ANTITOXIN.

Years	Cases	Deaths	Mortality per cent.
1895	4521	1424	31.4 %
1896	991	460	46.4 %
1896-1897	995	335	33.6 %
	6507	2219	34.1 %

DIPHTHERIA TREATED WITH ANTITOXIN.

Years	Cases	Deaths	Mortality
1895	19,619	3163	16.1 %
1896	19,630	2684	13.6 %
1896-1897	5.382	675	12.5 %
	44.631	6522	14.6 %

These figures show a reduction of mortality from 34.1 % in pre-antitoxin cases to 14.6 % when antitoxin was used.

In the Metropolitan Asylums Board Hospitals the average death rate of the 7 years prior to using antitoxin was 35 %, while the average mortality of 7 years during which the serum has been used was only 15 %. ... ...

Generally speaking where Antitoxin is used on the

1st day of the disease recovery may be relied upon.

2nd " " " " a mortality of 4% may be looked for.

3rd " " " " a mortality of 10% " "

4th " " " " a mortality of 17% " "

5th " " " " a mortality of 25-30% " "

MacCombie (Report.Met.Asyl.Board 1903) shows that from 1897-1903 the total number of cases of Diphtheria treated at the Brook Hospital was 4812 without a death among those injected on the 1st day Goodall (Brit.Med.Jour.1899 Vol.I p.197) gives interesting statistics gathered from various hospitals showing the value of antitoxin in Laryngeal Diphtheria treated by Tracheotomy. In 8927 cases Tracheotomized and treated without serum the recoveries were28.4% while in 2374 cases Tracheotomized and treated with antitoxin the percentage recoveries rose to 63.4%

SERUM PROPHYLAXIS.

Persons exposed to the infection of Diphtheria may have immunity conferred on them for the space of 2 or 3 weeks by the use of Antitoxic serum. This protection may be however lengthened by repeating the injection of serum. For immunizing purposes smaller doses are sufficient 300-500

units according to age and bodily stature.

Jacobi cites Slawyk's report (Deutsch. Medicini Woch. 1898 No. 6) as emphasising the utility of serum prophylaxis. In certain divisions of the Charité Hospital of Berlin relapses of Epidemic outbreaks were common in spite of preventative measures till immunization was resorted to. The dose was 200 units repeated every 3 weeks. In this way the place remained free from Diphtheria. By way of experiment immunization was discontinued for a month when three cases of diphtheria occurred one of which was fatal. The injections were therefore renewed and during the following 2½ months up to the time of publication of the report no new case had occurred.

Zuppinger (Preventative Antitoxin Treat. Wiener Klinische Wockens. Vienna) in reviewing the experience of others in various other countries presents his own. Out of 1000 children exposed and treated by preventative injections of antitoxin only 18 developed the disease. Of this number he believes 11 had already contracted diphtheria as the symptoms developed at once. This leaves only 7 cases in which the serum failed to protect. Naturally one must, in appraising the value of such statistics, take into ... ...

consideration the fact that a certain number of children exposed to the malady would not develop the disease whether treated with serum or not unless the bacilli find in them a suitable soil as regards lowered vitality. Still there seems to be little doubt of the value of prophylactic injections and this more especially in Children's hospitals where ordinary methods had failed to localize the cause of mysterious outbreaks.

Ibrahim (Deut.Med.Woch.Mar. 16.05) deals with the same question. This author has used injections on children in hospitals. He divides his observations into various headings. First he employed serum on the brothers and sisters of patients admitted into hospital suffering from diphtheria. They were injected at their own homes, he found that in not a single instance did an immunized child contract infection.

Secondly he injected the children in the ward where diphtheria turned up accidentally, in the case of the injected children no further infection occurred

Thifdly he used the serum in cases of mixed infection. Here the other children were Immunized as soon as it was necessary to admit a child

suffering from Diphtheria and measles or Diphtheria and scarlatina, into a measles or scarlatina ward Only one child thus immunized contracted the disease. He also admitted some children into diphtheria wards who were not suffering from this disease and immunized them, in no case did infection occur. He used doses of 250-300 units and would repeat this in two weeks where measles children are exposed to diphtheria but in 3-4 weeks in other cases will suffice.

In certain districts of Nottinghamshire recently proposals have been made by M.O.H. to the local Authorities to provide serum to be used as a prophylactic measure in persons known to have been exposed to infection. Initial expense is the great drawback and on this account such proposals are generally rejected. Still if by such means, and the above reports confirm the value of the proceeding, the M.O.H. should be able to check an outbreak of the disease the gain to the authorities would certainly in the end outweigh the initial outlay. Such measures have been used with success in Essex (Porter.Leeds and West Riding Med.Chir.Soc. Ap.22.1904) Cambridge and in the States. Park (Loomis - Thomson, Surg.Pract.Med. Art.Diph) shows the value of this Prophylactic measure in America

He gives records of 1043 cases many of which occurred in Tenement house population. In a large percentage of the whole number diphtheria bacilli were found in the Throat when the serum was administered, and all had been exposed to diphtheritic infection under conditions more or less favourable for transmission of the disease Amongst those immunized only 3 cases of Diphtheria occurred between 1 and 30 days after the treatment one on the 12th, 17th and 19th days respectively Park has summaraized the 1045 cases as follows:--

(see next page)

Name of Hospital	No.of cases Immunized	No.of units of antitoxin administered	No.of cases of D. developing among those immunized between 1 & 30 days	No.of cases developing within 24 hours	No.of cases developing after 30 days	No.of cases of D. that occurred in the institution prior to immunization.....
New York Infant Assylum 1st immunization	224	100-200	1 mild 19th day	0	6	107 cases in 108 days
Ditto 2nd immunization.....	245	125-225	1 mild on 12th day	0	4	6 in 12 days
Nursery & children's hospital	136	50-200	0	0	0	(46 in 90 days (15 in 15 days
New York Juvenile Assylum	81	150-250	0	0	0	12 cases 3 days
New York Catholic Protectory	114	150-600	0	1	0	5 in 3 days
Bellvue Hospital.....	11	175-225	0	0	0	2 in 10 days
Health Department.Inspectors	232	150-250	1 mild 19th day	3	3	1 or more cases in more than 90 families.
Total	1043	----------	3	4	13	

SECTION II

GENERAL MEDICINAL AND LOCAL TREATMENT OF DIPHTHERIA.

Patients with diphtheria must be isolated and if treatment is to be undertaken at home precautions should be taken to prevent infection spreading to others; and other members of the family are to be placed in quarantine and forbidden to attend church and other public assemblies. The best ventilated and lighted room will be chosen for the patient and preferably one with as much sun as it is possible to obtain. From this room all furniture, carpets, and hangings which are not absolutely essential should be removed and a large sheet saturated with Carbolic acid, Izal, or other disinfectant is to be hung over the door of the apartment. All expectoration membrane etc. should be received in old rags and immediately destroyed by burning. Rest in bed is essential and all important as a preventative of the sudden cardiac syncope, which is apt to supervene on exertion during an attack. For restless refractory children raising the foot of the cot on blocks of wood will aid in quietening the

patient and at the same time assists the work of the heart. Patients exhibiting signs of Toxaemia, albuminuria, and a fast irregular pulse require careful watching and strict recumbency enforced. The local exudate should have disappeared and the circulation should be normal before a case be allowed even to sit up in bed. Light nutritious food is to be administered in frequent small quantities, milk, beef tea, eggs etc, Mild cases may be allowed ordinary diet in about a week's time. Cases early treated by antitoxin do not in my experience develop albuminuria. In any case unless the urine be scanty, albuminuria does not seem to contra indicate small quantities of beef tea an occasional egg in the dietary. Raw meat juice, if the patient will take it, will be found to act beneficially in cases of marked pallor.

Aperients require care on account of the necessary movements attending their exhibition and they sometimes give rise to troublesome vomiting. Constipation if present is best met by small doses of calomel followed by a saline; enemata are also useful.

Nasal feeding may have to be undertaken where diglutition is difficult. Repeated vomiting

demands rectal alimentation of peptonised milk containing perhaps a little brandy. In ordinary cases water may be allowed ad libitum to allay thirst and flush out the kidneys, small pieces of ice slowly sucked will have a soothing influence on inflamed fauces and alleviate much distress. Amongst drugs two especially stand out pre-eminently useful in the treatment of diphtheria, viz: Iron and Strychnine. The former, amongst older physicians, was a sheet anchor. In the early stages however it is best avoided as it causes troublesome dryness of the mouth. The form for administration is generally as Tinct. Ferr. Perchloridi, which in varying degrees is antiseptic germicidal and blood restoring. Iron has been used empirically for its specific tonic effect in adynamic diseases notably erysipelas and diphtheria. The explanation of its value may partly be due to the chemical changes in the body giving rise to a certain amount of free Chlorine which circulates in the blood as an antiseptic, also the increase of iron in the Haemo-globin of the red cells increases their oxygenating power. Iron should be given in large doses and at frequent intervals - a child of say 7 years may have ℥ii or ℥iii in

24 hours, given every couple of hours. Glycerine makes the mixture more palatable. It is contra-indicated in cases where severe vomiting is present as it may increase the gastric irritability.

Strychnine is a valuable remedy in combating the action of the Toxines. It is a stimulant of the vasomotor and respiratory centres and has a great affinity for motor nerve centres, and these are parts which are attacked by the Toxines of diphtheria with directly opposite effects. It should be given in substantial doses, children will take as much as ½ gr. per diem for several consecutive days without any but beneficial results. Its utility in cardiac complications is referred to later. After a few days strychnine may be advantageously combined with Tr. Ferr. Perchlor. and by its action on the bowel tends to obviate the constipation which the Iron induces.

Digitalis is better avoided owing to the tendency to cause sickness. Strophanthus is useful in cardiac depression. Alcohol in the form of Brandy should be freely exhibited in all severe cases especially if pallor is becoming evident with a weakened first sound. If the stomach is ~~vom~~ irritable

iced champagne may be given instead.

Potassium chlorate is a drug which has long been used in treating Diphtheria and has still many admirers. But as the drug tends to weaken the patient and injure the kidneys, if used at all caution must be exercised. It may be combined with the Tr.Ferr. Perchlor.

Local Treatment. According to the accepted views relating to the Etiological and pathological connection between the Local affection and the resulting systemic condition in diphtheria it is obvious that considerable benefit is likely to accrue from vigorous local applications at the site of disease. The throat may be painted at frequent intervals with Glycer. Acid. Carbolici or Boracici: or various gargles may be employed in older children and adults. Potassium chlorate in gargle is warmly advocated by many. But their use is somewhat limited, children cannot be taught to gargle efficiently, and adults must - to do it properly - assume an upright position which may be harmful. Moreover in refractory children more harm than good may be done by persiting in fruitless struggles over local applications.

In nasal affections I have found great benefit and comfort given to the patient by using a nasal douche of Glycothmoline: whichever local application is used care must be exercised not to use any such as will cause local destruction of tissue and so be conducive to freer action of the bacilli and entrance of their Toxines: caustics therefore are bestbavoided altogether. One of the most efficacious local applications is Loeffler's solution consisting of Menthol alcohol and creolin applied to the membranous patches for a few seconds every 3 or 4 hours.

In treating Ocular diphtheria mild antiseptic irrigation should be employed and this frequently. For this purpose Boracic Acid 10 p to the 3 I of water is most suitable or 1 in 10,000 Perchloride of Mercury lotion. Iced applications to the lids at first and later warm fomentations are gratifying. If membrane be present on the conjunctiva the application of Nitrate of Silver (10 gr. to the ounce) may be used provided the conjunctiva bleeds easily and is succulent otherwise there is a risk of contraction of the lid afterwards. Its action is neutralized with sodium chloride solution.

Another suitable lotion is Sulphate of Quinine gr iii to the ounce.

SECTION III

TREATMENT OF LARYNGEAL DIPHTHERIA

Should any signs of Laryngeal trouble arise a steam tent should be erected over the bed, this gives considerable comfort to the patient, the steam may with benefit be impregnated with soothing antiseptics such as Tr.Benzoini Co.or Eucalyptus. For the restlessness small doses of opium give great relief and if combined with early serum treatment will delay or avoid in certain cases, the necessity for recourse to operative interference. Cyanosis will contraindicate opium, but this is a remedy which warrants an extended trial especially where the parents or friends are adverse to operative measures. The rest induced by the opium tides over a dangerous period during which the serum may not yet have been absorbed or become effective. The dose of the Tinct.Opii recommended is a number of drops equal to the child's years of age. Should however the restlessness increase and cyanosis become more marked, or frequently recurring paroxysms of dyspnoea with recession of the intercostal spaces and epigastrium supervene then we

must face the question of giving relief by Tracheotomy or Intubation. My experience of Tracheotomy in severe laryngeal cases has been a fortunate one as the following cases which came under my personal care in hospital and private practice will show. Intubation has not in this country attained the favour which has been accorded to it in the United States and on the Continent. My opinion is that for the general practitioner at least Tracheotomy is the safer and best operation, for after intubation one requires almost constant medical supervision in case the tube be extubated: and this is not always practicable where the practitioner may reside at a distance from his patient. A skilled nurse is generally able to attend successfully a Tracheotomy case but would be helpless in the event of a tube being extubated after Intubation. In addition the facilities for medical men acquiring the manipulative skill necessary for intubation are naturally difficult to obtain. Bungling and forcible attempts at introducing the tube will damage the larynx and perhaps lead to false passage. Again, the exertion of struggling during the performance of intubation might be fraught with danger of cardiac syncope.

In my experience very little anaesthetic is required for tracheotomy so that this can scarcely be considered a serious objection. In certain cases too where membrane is present low down in the larynx and in the Trachea Intubation may have to be followed by Tracheotomy. The idea of a "cutting operation" is considered by some as an objection but in such extreme cases this adds but little more to the anxiety of the parents. The keynote to success in Tracheotomy is that the case be not left too long before the operation is undertaken, if the child is getting progressively worse far better to operate while yet there is sufficient time for the operator to complete Tracheotomy without undue haste. The following case which occurred in my practice a few months ago will serve to illustrate the main points in connection with the operation and after treatment. A well trained nurse is essential if the case be treated in a private house for on her skill and attention depends to a great extent the success of the case.

Case 1. L.B. aged 4 years, Female, seen on January 9th, had been ill with what the parents

considered Bronchitis for 4 days before seeking advice. The child was a well nourished girl with a short stout neck. She was pale and had an anxious expression - Temp.100° F. Pulse 128 per minute - respiration 32 - The inspiration was not markedly croupy the lower chest wall being slightly retracted - there were rhonchi and a few crepitations generally over the chest especially on the bases. The tongue was thickly furred. On the tonsils and soft palate there was a moderate degree of exudation, the cervical glands were enlarged, a few crusts were visible in the nostrils some of which had been picked off leaving raw excoriations. A tent was erected over the cot and an extemporaneous steam kettle got ready.(I find in emergencies a thick piece of stout brown paper rolled into a tube and attached to an ordinary kettle forms a fair satisfactory substitute for a steam kettle.) 2000 units Antitoxin were given in the subcutaneous tissues of the back at 5 p.m. and a diaphoretic mixture ordered. At 8 p.m. on my second visit as there was no improvement a further dose of 2000 units was given. The retraction was becoming more marked in the epigastrium and interspaces, the pallor had added a cyanotic tint, the child was

bathed in perspiration the dyspnoea being very urgent. Some difficulty was experienced in convincing the parents of the urgency of the case and two hours of valuable time were lost during which the surface of the body was beginning to get cold and livid the child was obviously sinking. After a hurried consultation a table was got ready and a small quantity of anaesthetic was administered by a brother practitioner. The head was extended and held by the anaesthetist rigidly in the same position; a pint bottle wrapped up in flannel being placed beneath the neck to render the trachea more prominent. The incision extended from the cricoid cartilage to within ½ inch of the sternum - the skin and fascia were divided and the pre-tracheal muscles rapidly separated with the handle of the scalpel when a mass of veins was encountered some of which were pulled aside, but as the child had by this time practically ceased to breathe no time was lost in opening the trachea which was pulled to the surface of the wound by a sharp hook fixed in the cricoid cartilage. Fairly free venous haemorrhage occurred which however soon ceased after the tracea was opened

and respiration established: the insertion of the outer tube caused violent coughing and a good deal of membrane was expectorated through the tube, respiration became much quieter and a healthy glow pervaded the countenance in a few moments. The child was replaced in its cot and the steam resumed. Light nourishment was readily taken and the after history was somewhat uneventful. The nurse carefully attended to all expectoration through the tube frequently taking out and cleansing the inner tube. Warm moist gauze steeped in 1 in 60 carbolic was placed over the neck. After the operation the pulse was 120 Respiration 28: Temperature 100° F. On January 10th 2000 units serum were given. Temp. 99.8° F — Pulse 116. Resp. 30. The child slept the greater part of the time, the breathing was tranquil. Milk and brandy were given Milk half an ounce every hour and Brandy 3 i every 3 hours, Liquor strychnine m.½ every 4 hours. 11th January, the cough was rather troublesome mucus and small quantities of membrane were expectorated. Nourishment as before: no sickness: Temperature 98.8° F. Pulse 100: Respiration 32: 2000 units serum again administered. Outer tube taken out, cleaned and re-inserted.

January 12th. Child much improved. Still expect-

orating mucus and very little membrane through tube. No exudation seen on Tonsils or Palate: Pulse 80. Temperature 97.8 Respiration 28. 2000 units again given. Sleeping well and taking nourishment freely, an egg allowed with the milk and a small quantity of beef tea.

January 13th: Restless during the night and cough troublesome - no membrane was expectorated only mucus. January 14th: Outer tube removed and left out: Breathing very quiet, cough better: Pulse 80 Respiration 24: Temperature 97.8° F.

The subsequent progress was uninterrupted except for some cardiac irregularity, which however caused no undue anxiety. Earache was troublesome during the later part of the convalescence: No difficulty was encountered in getting the child to resume talking. She was allowed to sit up in bed on Jan.22nd and was up and dressed 10 days later. A mixture of Iron and Quinine helped to complete the convalescence. The wound in the neck healed kindly without trouble.

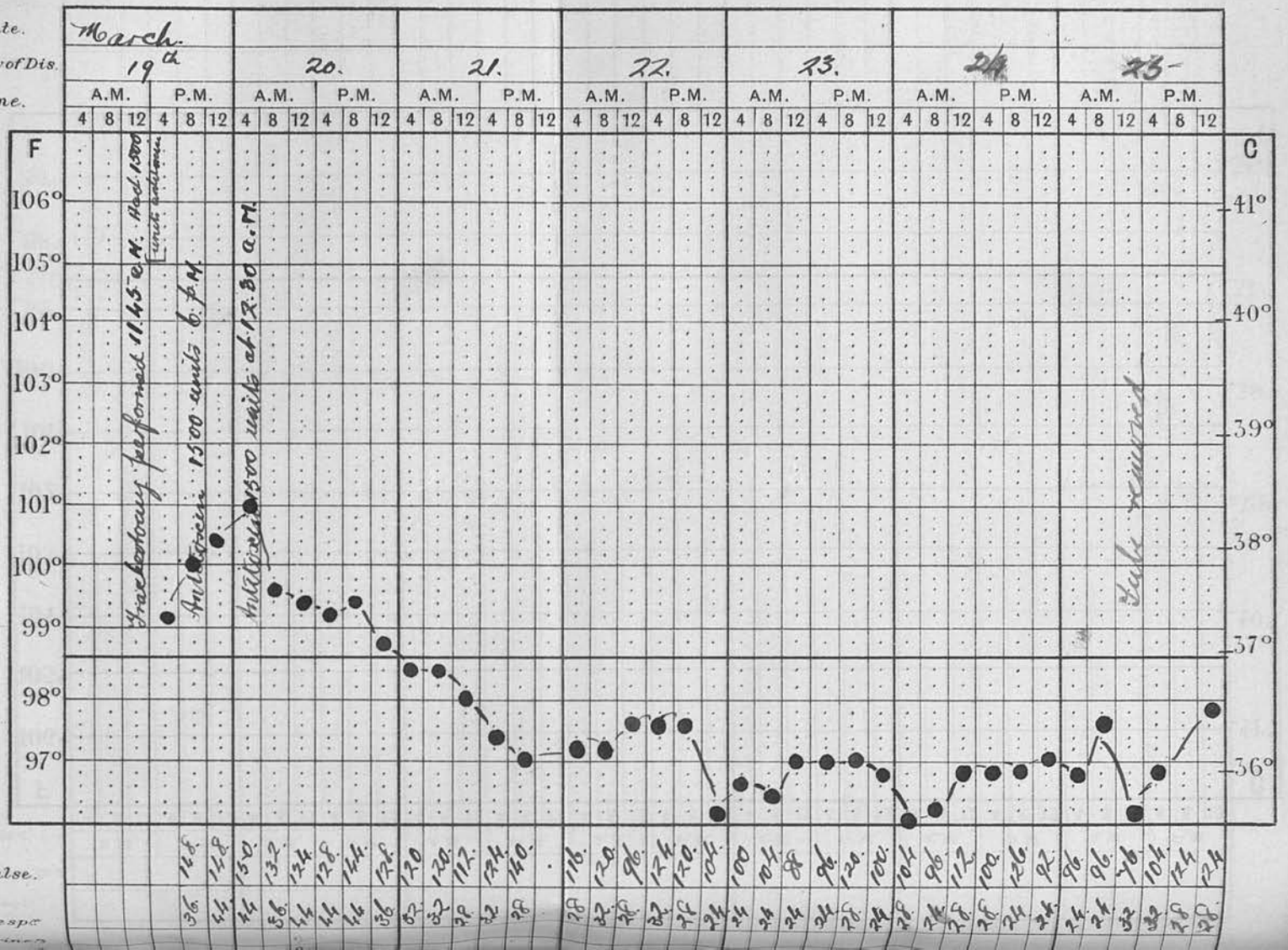
Total amount of Antitoxin given - 8000 units.

Case II N.C. aged 2 years: Male: Admitted into Dundee Royal Infirmary - March 19th 1900: Illness

said to have begun with a bad cold in the head two weeks prior to admission. There had been a croupy cough for two or three days. The breathing became distressed on the 18th, and got much worse during the night. On admission 11 a.m. Child was in a very dyspnoeic state cyanosed and showing considerable retraction of the chest wall on inspiration. The Tonsils and palate showed a a dirty grey membrane adherent to the subjacent structures Pulse 148: Temp: 100.4° F. Respiration 36. Urine contained albumen.

Tracheotomy was performed without delay owing to respiratory embarrassment, and followed by 1500 units antitoxin. This was repeated at 6 p.m. and again the following morning. The child was put in a steam tent. The operation was conducted under any but the most desirable conditions, as there was no time for cleansing the child, breathing ceased dufing the operation but was restored, after stimulation of the Trachea with a feather, by artificial respiration. A considerable amount of membrane was coughed up through the trachea after the operation. The temperature quickly

Name Norman Curie Age 2 Ward 2. Register No. 2760.



To face p. 163

subsided on the following day and on the 2nd day after operation was subnormal. The pulse also showed a steady fall in rapidity from 148 per minute on the day of admission to 96 on the 5th day after operation. The albumen was small in amount and was not detected four days after admission. There were no complications. The antitoxin was discontinued after the 3rd day because the exudate had gone from the throat and no further membrane was expectorated through the tube. Also the pulse and temperature and general condition were satisfactory.

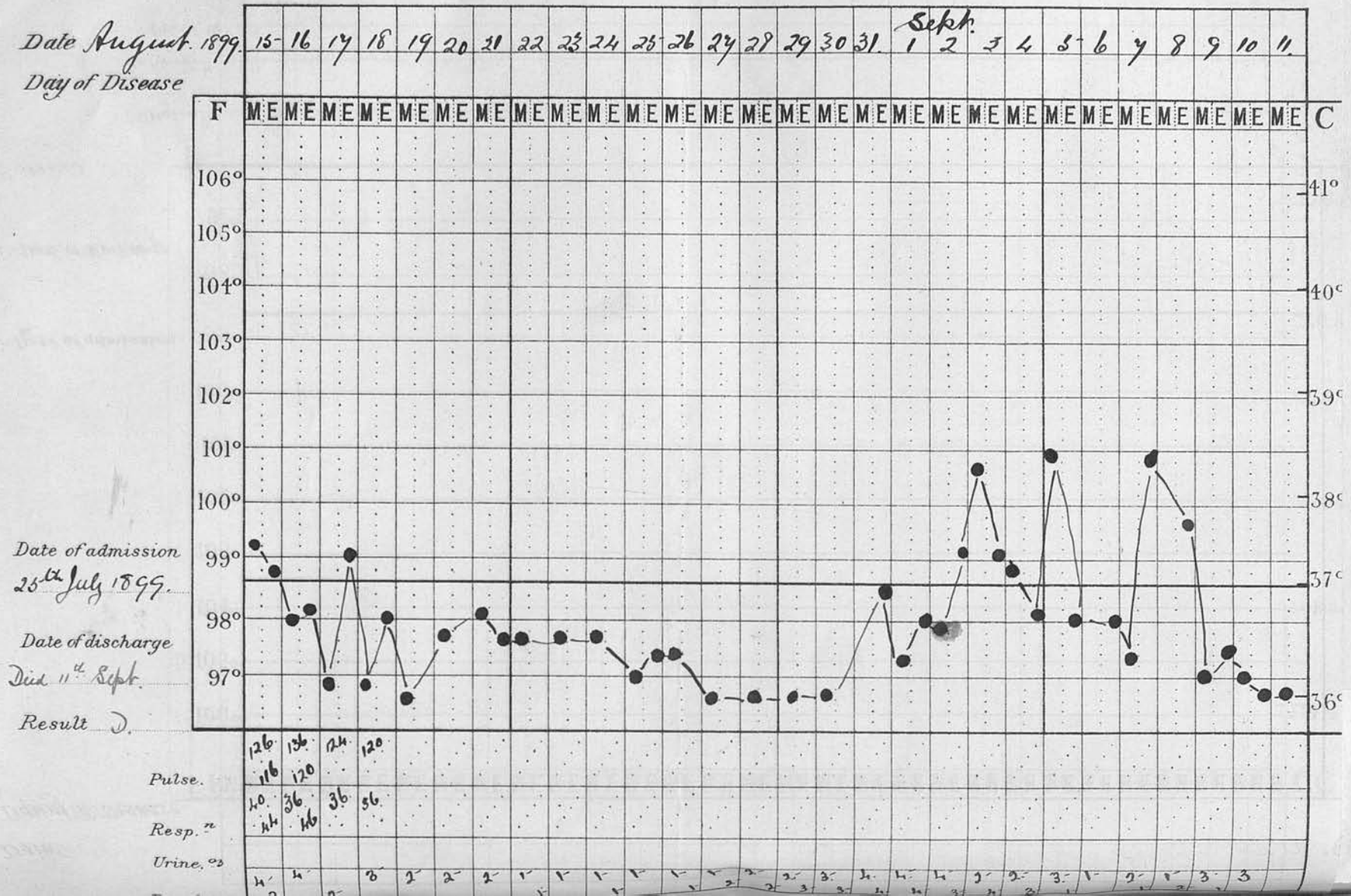
The tube was finally removed on the 6th day after operation: Feeding presented no difficulty and sickness was absent. On March 31st the child was quite well and was discharged on April 9th, twenty one days after admission.

Total amount of Antitoxin 4500 units.

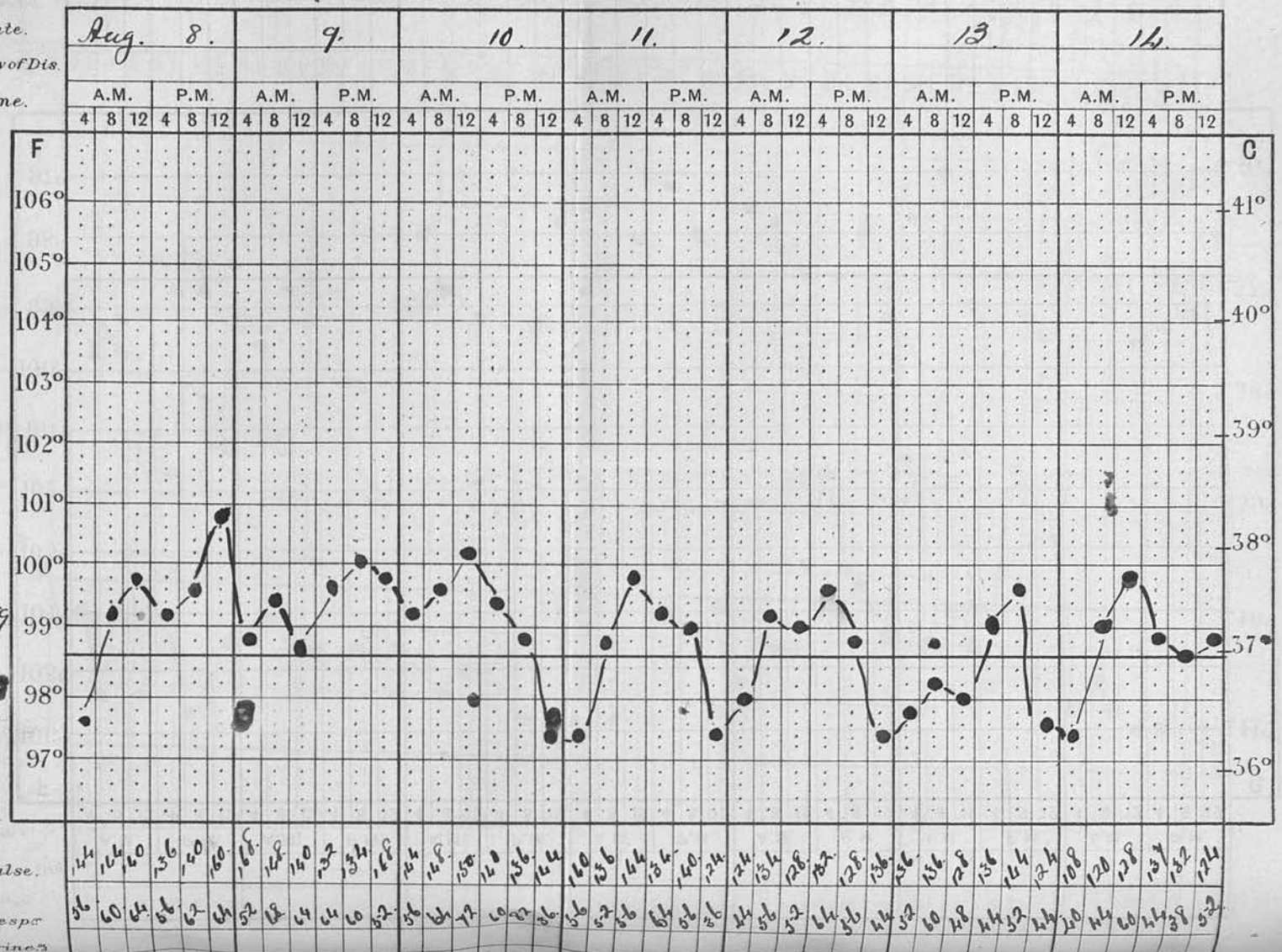
Case III

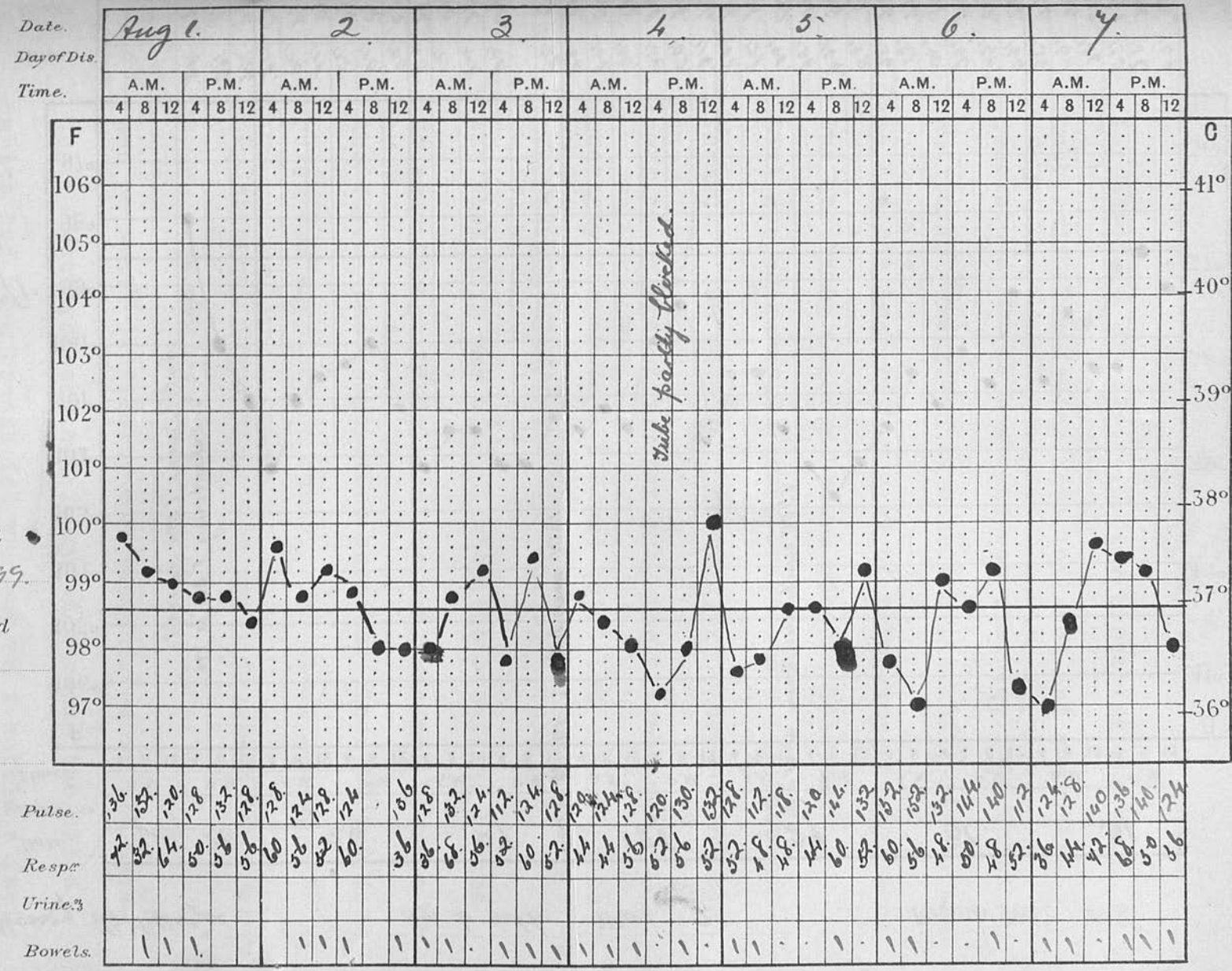
H. McK. aged 6 months: Male: admitted July 25th 1900. Child had been ill since July 21st with a cough which gradually become "Croupy" and on the 25th was so bad the case was brought to Hospital

Name Henry McKenzie Age 6 mths Ward 2. Register No 812.



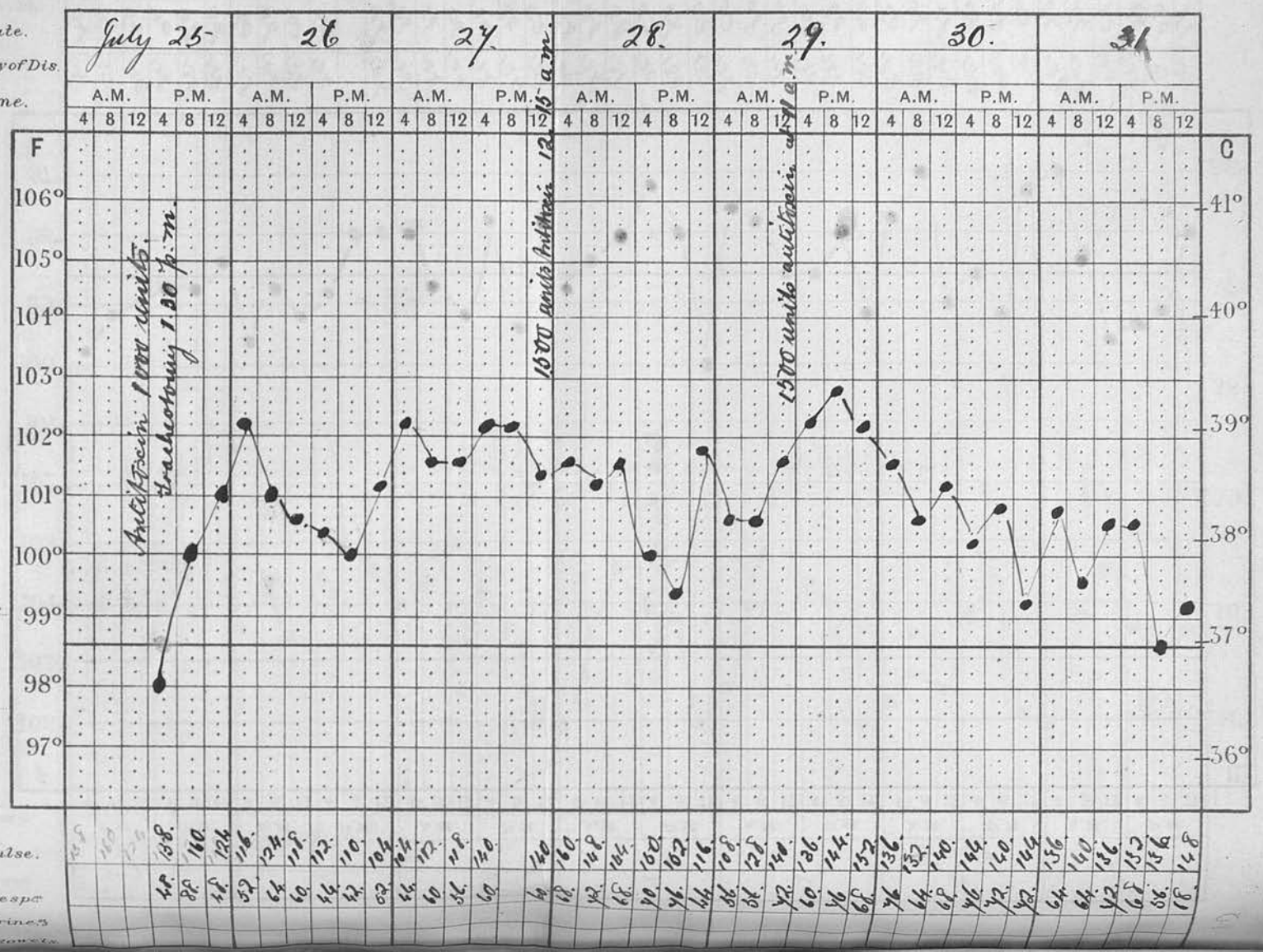
Name Henry McKenzie Age 6 mths Ward 2 Register No. 812





The tube was removed on the 6th day after

Name Henry McKenzie Age 6 mths Ward 2 Register No. 812.



To face p. 166.

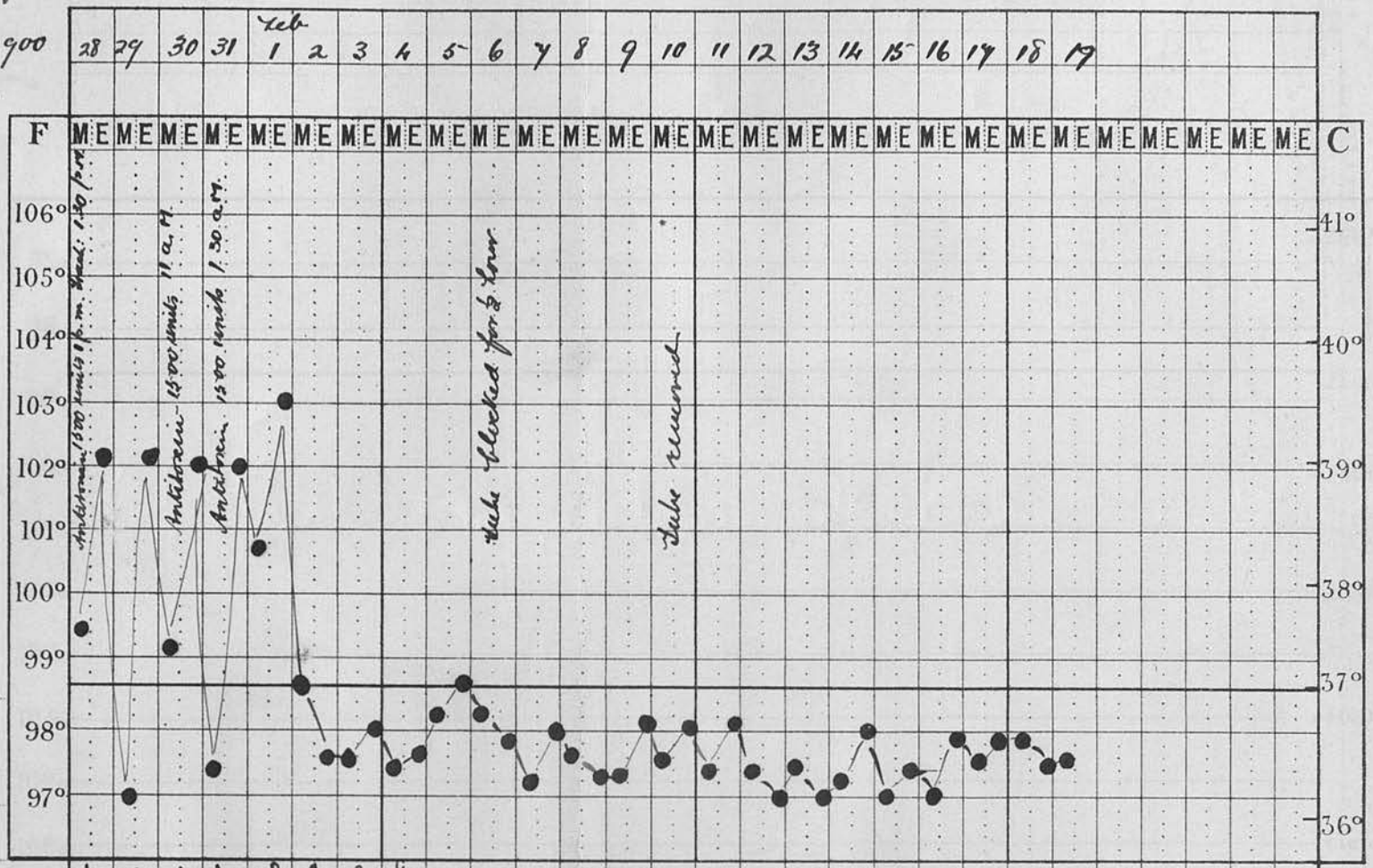
Admitted
25 July 1899.

Discharged

Result

for advice. On admission the breathing was very laboured. The fauces were inflamed and somewhat oedematous but no membrane was visible: 1500 units antitoxin were given at once and the child put to bed in a steam tent with a view of relieving the dyspnoea. The breathing however became progressively worse till cyanosis was evident, Tracheotomy was then performed. The case was interesting on account of the very young age of the patient, the trachea was scarcely larger than a goose quill and considerable trouble was experienced in getting a tube into it but when this was accomplished the breathing became so easy the child fell asleep and remained so most of the day. The temperature remained elevated and the pulse and respiration rapid. The chest showed patches of Catarrhal pneumonia. The small tracheal tube was frequently blocked up by small pieces of membrane and no small difficulty was encountered in the nursing. Matters were not improved because the child which had been breast fed was put on a bottle a fact which no doubt contributed toward the final disaster on September 11th from Gastro-enteritis and marasmus The tube was removed on the 6th day after operation. Total amount of Antitoxin 4000 units.

Name Mary Morrison Age 3 Ward 2 Register No 2314.



To face p 167

Date of admission
Jan 28. 1900

Date of discharge

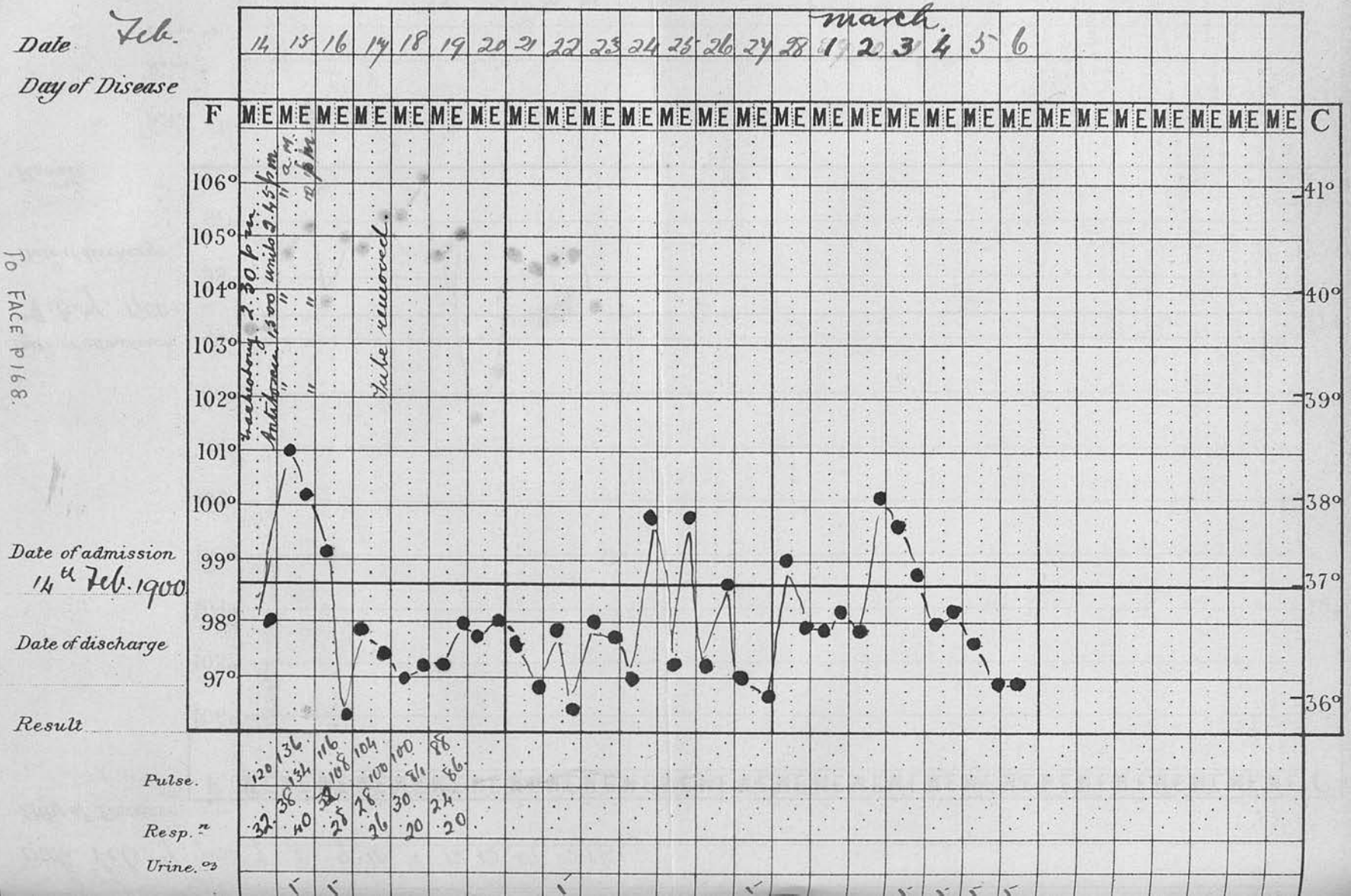
Result

| | | |

The temperature in this case which was subnormal on admission apparently from shock and Toxaemia rose after the operation to 102°F owing to the onset of the pneumonic condition. It remained about this figure for four days and gradually fell to the normal on the 8th day. No urine was obtainable for examination.

Case IV, M,M, aged 3 years. Female.
Admitted to Hospital on January 28.1900 as an emergency with urgent laryngeal obstruction. The palate Tonsils and uvula were covered with a typical membranous exudate. Cyanosis and recession of the interspaces and epigastric region were very marked. Resp. 44. Temp. 99'4°F Pulse 124. 1500 units antitoxin given on admission and Tracheotomy performed two hours later with great relief to breathing. The temperature was normal on the 5th day. The tube was finally removed on the 13th day some difficulty being experienced in getting the child to use his larynx. The tube became blocked a few days after operation and in spite of its removal urgent dyspnoea ensued which greatly frightened the child, fully half an hour elapsed before satisfactory respiration was established. Thereafter when the

Name Charles Keith. Age 3 Ward 2 Register No 2492.



To face p 168.

the outer tube was purposely blocked to encourage natural breathing the child was very nervous which accounts for the late date of its final removal. The case was discharged well on February 19th 1900

Total amount of Antitoxin given 4,500 units.

Case V C.K. Male : Aged 3 years. Admitted Feb.14. 1900 with urgent dyspnoea. The child had been ill and croupy for four days prior to admission.
Respiration trouble became worse the day before admission and no rest was obtained during the night. Child had measles two months before this illness and had never been well since.
On admission the fauces were clear. Cyanosis was commencing and considerable retraction of the chest wall was evident. Urine contained a trace of albumen. Tracheotomy performed on day of admission, operation uneventful: small amount of membrane expectorated 1500 units serum given at conclusion of the operation and 3000 units administered on following day after which the temperature rapidly fell to subnormal with a corresponding fall in pulse rate. The tube was removed finally on the 4th day and convalescence was uninterrupted. Discharged March 6th twenty days after

Name Ellen Smith Age 9/12 Ward 2. Register No. 1443.

Date.	Oct. 15	16.	17.					
Day of Dis.								
Time.	A.M. / P.M. (4 8 12 4 8 12)	A.M. / P.M.	A.M. / P.M.	A.M. / P.M.	A.M. / P.M.	A.M. / P.M.	A.M. / P.M.	A.M. / P.M.

F: 106° 105° 104° 103° 102° 101° 100° 99° 98° 97°

C: 41° 40° 39° 38° 37° 36°

Tachistony at 8.00 p.m. Antitoxin 1500 units @ 9.15 p.m.

To face p. 169.

Admitted 15th Oct. 1899.

Discharged

Result

Pulse.

Resp.

admission: No complications noted.

Total serum given 4500 units.

Case VI FeMale Age 9/12 months. Admitted October 15th 1899. Mother stated child had been treated in the Out-patient department but had no serum injections. One other child in family had mild Diphtheria lately. Progressive difficulty in breathing occurred beginning on the evening of the 13th. The case was admitted moribund from Toxaemia and dyspnoea. Palate and pharynx covered with membrane. The chest examination revealed signs of capillary bronchitis with impared basal resonance posteriorly. Tracheotomy was a "dernier ressort" and was performed immediately but did not give relief to the dyspnoea the child having little strength to cough. In spite of steam inhalations, brandy and serum hypodermically the child died 3 hours after operation. The post mortem showed that false membrane lined the trachea below the incision and extended into the bronchial tubes. The lungs showed ecchymoses on their surfaces and were Oedematous. Numerous patches of Broncho-pneumonia were scattered through their interior with attendant atelectasis the minute tubes being filled with a vicid blood-stained exudation.

Name Stephen Robinson Age 3½ mos Ward Register No

Date March

Day of Disease

	2	3	4	5	6	7	8	9	10	11	12	13	14
	1	2	3	4	5	6	7	8					

F C

106° 41°

105°

104° 40°

103°

102° 39°

101°

100° 38°

99°

98° 37°

97°

96° 36°

Antitoxin 2000 units

" "

" "

Tube removed

Tracheotomy

Date of admission Mar 2nd 1902

Date of discharge

Result

Pulse.	138 134	130 128	102 99	104 100	112 108	100 102	98 94	100 98	100 98	94 94			
Resp.ⁿ	32 34	34 36	30 28	30 24	26 20	26 28	30 26	24 22	22 20	24 22			
Urine &c													

TO FACE PAGE

Case :VII

S.R. Aged 3.6/12 years. Male: Admitted March 2nd 1902 suffering from severe laryngeal diphtheria. The child had been ailing with "sore throat and fever" for a week before admission. The cough and laryngeal obstruction developed on March 1st and gradually become worse. On admission there was a harsh respiratory stridor with moderate intercostal retraction. Cyanosis was absent. The child was put in a steam tent which gave a little relief. 2000 units Antitoxin were given at once. On the posterior pillar of the right side of the palate was a small membranous exudate otherwise the throat was clear. Urine showed no albumen. Later in the evening laryngeal stridor became more marked, restlessness increased and cyanosis made its appearance and by 10 p.m. recession of the epigrastrium and interspaces was so marked that Tracheotomy was performed and several pieces of thick tough membrane membrane were expelled when the trachea was incised. Dyspnoea disappeared and the child was comfortable in bed for an hour when the outer tube became blocked and had to be removed; great coughing followed and very rapid swelling of the tissues of the neck was observed so much so that the outer tube when re-inserted was rendered almost ineffectual in reaching the trachea. During the performance of the operation

note was made that there existed an unusually large Thymus gland bulging into the neck. The restlessness continued and for this 5 grains of Chloral Hydrade in syrup were administered and gave some relief. The Temp. was 101. 2° F. Pulse 138 per minute. Resp. 32 2000 units anti-toxin were repeated at midnight. During the early morning cutaneous emphysema appeared, beginning in the neck above the wound and rapidly extending upwards to the face scalp and eyelids also downwards over the sternum and chest wall to the abdomen. There were no signs of Pneumo-thorax. The child presented a peculiar bloated appearance, the eyelids being in a state of ptosis from invasion of the emphysema. This state of affairs lasted for a couple of days then gradually subsided and the child made a good recovery - the tube being removed for good on the 5th day. The temperature and pulse steadily fell to the normal. The nourishment which was easily taken consisted of milk, beef juice and a little brandy. The interesting feature of the case was the extensive emphysema due apparently to the tracheal wound being situated rather on the lateral aspect of

the tube which allowed the child to cough into his subcutaneous cervical tissues when the outer tube was coughed out and this was rendered easy owing to the enlarged thymus:possibly also the violent expiratory efforts of coughing may have caused rupture of one of the pulmonary vesicles though no pneumo-thorax was present.

Total amount -- Antitoxin 6000 units.

COMMENTS ON CASES DESCRIBED.

Age Recovery from Tracheotomy for Diphtheria is rare below the age of 2 years - The youngest case recorded was a child of six months (Medical Times & gazette 1880 Vol.ii p 593) Death in case iii aged six months recorded above was really due to intercurrent complications and difficulty from change in feeding during very hot weather. The child lived six weeks after the operation.

The average of recoveries after Tracheotomy for for membranous laryngitis is given as 19 out of 50 or 1 in every2.2/3rd cases: (Buchannan. Paris. Med. Congress 1881 Vol. 1:. P 208)

Dr. Lindner (Deut. Zeitsch. F. Chir. Bd. XVII Heft. 6) states that recoveries during the second year amount to 12%. In the third year they rise to 55%.

Dr. Passavant (Ann. of Surgery Vol. I. p,582)

gives 67 cases cured out of 229 or 1 in 4.

In the series of cases given above one of which (Case I) was in private practice 5 of the others were met consecutively during a term of residency at Dundee Royal Infirmary, and 1 (Case VII) at Lincoln Hospital the average age of the children was 2.4 yrs. The youngest, six months, died of Gastro-Enteritis. One child 9 months (Case VI) also died of Lung Complications. One child of two years made a good recovery.

DOSE OF ANTITOXIN GIVEN. Excluding the sixth case which died shortly after admission, the average dose of antitoxin in the remaining six cases was 5250 units. In no case was paralysis shown during the period of observation, but all except case I were not seen subsequently to their discharge from Hospital.

TIME OF OPERATING Case VI was moribund on admission and case I was delayed too long on account of the parents' obstinacy, in the others reliance was placed mainly on the amount of Intercostal Recession and sucking in of the epigastrium on inspiration; also on the appearance of cyanoses. Prolonged dyspnoea with epigastric recession in such cases

brings about an action on the lung surfaces analagous to that of a cupping glass on the skin viz: hyperaemia, stasis, hyper-secretion of mucus splenization and atelectasis (Passavant loc, supra cit. p 153) and Case VI. The character of the dyspnoea varies and is of importance in the prognosis after operation. In one class of case the respirations are hurried and urgent, are associated with great restlessness of body and loud stridor tending to indicate probably that the mischief is localised in the larynx and that the small tubes are patent. In such cases (V. VII) there is observed vigorous action of the extraordinary muscles of Respiration, sucking of the infra-costal and epigastric regions, and later of the supra-clavicular and supra-sternal regions. While this sucking in is vigorous and well marked the lungs are probably still free, and if auscultation can be performed the bases give a good vesicular murmur and are resonant to percussion, those being of favourable omen. In another class the dyspnoea is less urgent and has been slower in onset, restlessness has been less marked and less vigorous in drawing is observed especially in the regions above,

the chest being rather puffing or heaving en masse and that with difficulty. Auscultation reveals numerous small crepitations and percussion yields an unimpaired note, those serve to indicate the existence of mischief in the bronchial tubes with œdema of the lung and are thus much less favourable in prognosis. Case I was approaching this type and case VI typical of the condition. The chief danger of delaying operation too long are œdema of the Lungs, exhaustion of the Right Heart and Pulmonary Artery Thrombosis.

THE ACTUAL OPERATION

ANAESTHETIC. Chloroform has been the anaesthetic invariably chosen for children - it allays spasms and prevents struggling - very little is really required and even where cyanosis has been present it may be administered provided due care be taken.

SITE. The High operation was chosen andis most desirable and easier to perform than the low operation chiefly because of the comparatively superficial position of the Trachea. The Isthmus of the Thyroid gland generally crosses the 2nd or 3rd ring. In my experience it may be divided, without untoward results, during the operation in order to get sufficient room. The anterior jugular veins and

their branches are smaller at the upper part of the trachea but are generally prominent enough to give rise to considerable haemorrhage which however ceases as soon as the Trachea is divided and respiration fully established. The main objections to the Low operation are (1) The depth of the Trachea and its comparative mobility (2) Pus is easier led to the Medias-tinum and Broncho-pneumonia more apt to ensue. (3) The innominate artery and vein may be so high in the neck as to be wounded I have once known death result from wound of the vein during the operation owing to the head being too much extended and the vessel pulled into the lower part of the neck. (4) In stout children the Thymus gland may be large enough to give difficulty in retaining the tube (case VII)

TECHNIQUE When the patient is sufficiently anaesthetised antiseptic preparations should rapidly be completed. The main guide in the operation is the Cricoid cartilage, which must be clearly defined by the finger. The child's neck is rendered prominent by a sand-bag placed beneath it, the arms are fastened securely to the body by a bander which is not tight enough to obstruct the

already impeded respiration. The head is rigidly held by the anaesthetist in the middle line, the trachea is steadied by the operator's left thumb and forefinger. The skin is incised from the centre of the cricoid cartilage downwards for a couple of inches, care having been exercised to see that the wound does not tail at either end of the incision. Subcutaneous tissues fat superficial vessels and nerves are all divided in a similar manner . The interval between the sterno-hyoid muscles is then separated by the handle of the knife or a director: and the deep ~~fa~~ fascia is exposed and here the difficulty begins: It is important that this fascia be fully and freely divided, else one is apt to pass the tube between it and the Trachea which only leads to further embarrassment of Respiration. This fascia is also continuous with the pericardium below and may in unhealthy states of the wound lead pus into the mediastinum. I have found the best way of dealing with the fascia is to divide it transversely at the lower border of the Cricoid then to make a pair of forceps grasp the fascia vessels and isthmus of the thyroid (if in the way) on either side and divide the tissues between the forceps longitudinally, the incision being thus made T shaped. This

practically renders the hemorrhage nil and the upper two or three tracheal rings are laid bare. A sharp hook is next fixed in the Cricoid to bring the trachea to the surface of the wound: the knife being now held short and firm is plunged into the wind pipe which is incised from below upwards.

It is absolutely essential in small children to keep rigidly to the middle line, because of possible damage to the large vessels and care should be taken to see there is not the least twist of the neck during incision into the trachea, in which case when the neck is straightened great difficulty will be found in keeping in the outer tube. (Case VII) It is good practice also never to incise the trachea till this structure is actually felt with the finger or better seen though this in my experience is rare as some hemorrhage obscures the view. The greatest difficulty in my cases was Case III where the Trachea was so small and soft as to be difficult of detection. Few sounds are more joyful to the operator than the hissing noise of the inrushing air when the trachea is well opened and the subsequent cough and expectoration which ensue. And few sights are more gratifying than the immediate relief from dyspnoea and the rosy suffusion of the countenance which follows on the first few respirations. Immediately the trachea is incised a dilator is introduced and the wound held open

the ejected mucus and membrane are got rid of . It is then advisable to introduce a sterilized feather into the trachea and further stimulate the expulsion of false membrane for the more got rid of at the operation the easier will the subsequent nursing be. With the dilator still in situ, the outer tube with tapes attached, is introduced at first transversely to the incision and then rotated till the tube is vertical, in this manner the introduction of the tube is facilitated as one lip of the tracheal wound is depressed by the tube, allowing it to slip in readily. The tapes are then fastened round the neck, some gauze being packed between the flange and the skin. Perhaps a stich at the upper and lower angles of the incision may be deemed necessary. When respiration is tranquil the inner tube may then be inserted and the whole covered up with warm moist gauze which is constantly renewed.

After Treatment. The child is placed in a steam tent and carefully watched to see it does not try to remove the tube. The inner tube (which ought to be readily expelled by coughing) is frequently changed and cleansed by a solution of bicarbonate of soda. Feathers are kept handy to pass into the outer tube to aid removal of mucus or membrane. They are best avoided however if there be much whistling with the breathing indicat-

ing dryness of the trachea. Here a spray of Listerine or borax and soda may be used with benefit. Should there be any difficulty in swallowing owing either to the pressure of the tube, pain or paralysis the child may be fed by means of a soft catheter passed through the nose, but as a rule this will not be necessary.

DIFFICULTIES AND COMPLICATIONS OF THE OPERATION.

1. Insufficient skin incision leads to great trouble with the later part of the operation.

2. Departure from the middle line: wound of the larger vessels may result or if the trachea be very soft it may be missed altogether and the œsophagus opened instead.

3. Short thick necked childred are troublesome subjects especially when the Thymus is unduly prominent. (Treves Surg. Anatomy p154)

According to TILLAUX, the distance between the Cricoid cartilage and the sternum in a child of

3–5 years	is	1½ inches
6–7 "	"	2 "
8–10 "	"	2¼ "

4. Haemorrhage. This varies greatly and generally is not formidable. The veins are usually distended and engorged. These ought to be picked up and divided between forceps so far as is practicable and the deeper veins dealt with the fascia as described. If the case be urgent it is not necessary to delay

incising the trachea on account of even moderately free bleeding - but entrance of blood to any extent into the lungs is to be avoided (by turning the child on its side when the trachea is incised) for fear of setting up broncho-pneumonia.

5. Insertion of the Cannula. Generally results from insufficient division of the deep fascia.

6. No relief is obtained after the operation is truly performed and the Cannula in place, this is generally due to membrane blocking the trachea or bronchi below the site of operation or to the child being practically asphixiated before the operation is completed. The indications would be to stimulate expectoration by use of the feather and resort to artificial respiration. If the feather fail a catheter attached to a tracheal aspirator may be tied as was done in case VI but without success.

7. Emphysema, cutaneous as in case VII or deep emphysema. Dr. Champney's (Trans. Med. Chir. Soc. Vol.LXV, LXVII and LXVIII) discusses the subject of deep emphysema and concludes that "emphysema of the anterior mediastinum, often associated with pneumothorax, occurs in a certain number of tracheotomy cases, the conditions which favor its occurrence being division of the deep cervical fascia, obstruction to the air passages and inspiratory efforts. The dangerous period during the operation is in the interval between division of the deep fascia and the efficient introduction of the Tube."

The tube I have used in all my cases was either an ordinary curved tube (Edinburgh pattern) or the bivalve tube. Should any sign of ulceration of the trachea appear through irritation of the lower end of the tube an angular Parkers tube should be substituted or a rubber substituted. A diameter of

6 m m is suitable for children 1½-4 yrs of age
8 m m " " " " 4 -8 "
10 m m " " " " 8-12 "

The tube should be removed at the earliest possible opportunity either altogether or to be replaced by a rubber substitute. The expectoration of frothy blood stained mucus is an indication of irritation and commencing ulceration of the trachea. Apart from the risks of this ulceration the longer a child is allowed to use the tube for breathing through, the more is the act of natural respiration difficult to establish, it being as it were forgotten. I have generally used a tube with an aperature on the upper aspect or a bivalve outer tube, so that the child may be taught as early as possible its usual breathing by placing the finger on the flange of the tube. When this lesson is satisfactorily learned the sooner the tube is removed the better.

In my series of cases

Case I. had the tube finally removed on the 5th day.
2. " " " " " " "
3 " " " " " " "
4. " " " " " " "
5. " " " " " " "
7. " " " " " " "

6th day
6th day
14th day
4th day
6th day.

The conditions which may impede removal of the tube may be - that the function of larynx in a young child has fallen into abeyance. Paralysis of the

vocal cords or closure of the Trachea or larynx by granulation.

Patient persevering efforts to coax a child to talk or in younger subjects to blow a trumpet will generally overcome the difficulty, but when the use of the tube seems likely to become protracted the larynx may be dilated - a step easily accomplished as it is rarely blocked but usually only functionless from disuse. After giving a whiff of chloroform a catheter is passed upwards from the tracheal wound through the glottis and made to emerge at the mouth. This left in situ for a day or two (the tracheotomy tube being also in place) when after withdrawal of the cannula from the trachea the catheter can usually be dispensed with. In more obstinate cases McEwans tubes passed through the larynx into the trachea below the wound should be employed.

Copetii (Gazz. degli Osped. April 1 1906) discusses the persistence of laryngeal stenosis after tracheotomy and incubation in 1200 cases of diphtheria: of these primary tracheotomy was necessary in 25 and secondary tracheotomy in 94 of the cases. 300 cases were intubated. Post operative stenosis persisted in 40 cases. The difficulty in many was purely

mechanical (granulations pressure of glands etc.) or due to the grave pulmonary or cardiac complications present. In 10 cases these explanations were not enough to account for the condition. Those Copetii divided into two groups 1. Where the stenosis was due to a constitutional condition of "Spasmophilia" associated with a ricketty or tuberculous diathesis. 2. Where the spasm was due to reflex pulmonary irritation for example foci of broncho pneumonia.

Complications attending the after treatment of cases of tracheotomy may be:-

1. Haemorrhage, which is rare - and due either to ulceration of the trachea, separation of false membrane by sloughing or from granulations. Cases are recorded of ulceration into the innominate artery after low tracheotomy in children (Trans.Path.Soc. Vol. XI p.20)
2. Sloughing of the wound. also rare and usually prevented by gauze between the flange of the cannula and the skin and also by maintaining antiseptic precautions.

3. Ulceration and stenosis of the trachea caused by faulty tubes. In diphtheria the tissues are below par as regards resistance and so are comparatively easily ulcerated.

4. Mediastinal supperation - this may be caused by a descending cellulitis from the wound. This is a serious and usually fatal complication.

5. Broncho-pneumonia as indicated by a rise of temperature, dyspnoea, crepitations on auscultation, and percussion dulness at places when the lungs are examined.

Dhomont (Le Progrès Médical Feb. 16.1907) gives the opinions of several observers especially Landouzy who think the lot of children who have undergone tracheotomy is extremely precarious and that they largely contribute to tuberculosis and pulmonary affections and that few of them grow up. In 9 cases operated on by Dhomont he was able to follow 4 of them to adult life and those were all healthy. Tissier has followed up 10 cases, 2 have died of tuberculosis, one of whom lived to 25 years was operated on at the age of 3 years. The other died at 16 years. A third case has laryngeal phthisis and a 4th is in the last stage of Phthisis: the others are all well.

Intubation which is the operation universally practised in America and on the Continent is now gaining

favor in Hospital practice in this country. The procedure is viewed more favourably because no cutting operation and no anaesthetic are required. When constant supervision is possible undoubtedly many cases of Laryngeal diphtheria will be best treated by Intubation. On the other hand certain cases which are intubated will ultimately require to be tracheotomised, it may be because the Intubation tube is constantly being coughed out or because no relief is gained by Intubation on account of the false membrane extending so low down in the larynx and trachea. It is probably best avoided and indeed inadmisable in cases which are in extremis from suffocation when brought under observation and when toxaemia is very marked, in these cases tracheotomy is more likely to give relief from suffering during the patient's last moments. Where there is severe faucial and nasal involvements with tonsillitis and enlarged cervical glands tracheotomy will be the best operation, because it is more likely to give relief to the dyspnoea and also because in such cases the tissues may be so soft that ulceration may easily be caused by the Intubation tube. Probable oedema of the larynx too which will render insertion of the tube specially difficult will decide in favour of tracheotomy.

Intubation was first adopted by Bouchut in 1858 but it fell to Dr. O'Dwyer of New York to perfect the necessary instruments and also to demonstrate the utility of the operation. O'Dwyer began devising his instruments in 1880 but several years elapsed before his present day set was perfected. The tubes originally were made of white metal plated with gold, but later were constructed of hard rubber over-lying metal, those being less likely to injure the larynx and being lighter are more readily coughed out should the lumen become occluded by flase membrane.

TECHNIQUE.

The child must be under perfect control and may either be held in the upright posture or laid on its back. Having chosen the proper sized tube for the child's age and inserted a piece of silk into the eyelet, it is attached to the introducer. A gag is inserted into the mouth, the left forefinger clearly defines the epiglottis and pulls it well forward towards the base of the tongue. The tube is then slipped over the dorsum of the tongue and is guided by the left forefinger into the chink of the glottis. The tube is then pushed off and the obturator withdrawn, the tip of the finger still holding the head of the tube, to prevent its being

pulled out. Its presence in the larynx is known by the relief to the dyspnoea and the shrill metallic cough which ensues. Should the Oesophagus receive the tube no relief is gained and the silk will grow progressively shorter as the tube is swallowed, in which case it must immediately be withdrawn and another attempt made. After a successful introduction the gag is removed and the child allowed time to cough and expectorate. The silk thread may then either be cut away or attached to the child's ear by a loop. In older children who have got their molar teeth and who may perhaps chew the thread thus left it may be advantageous to bring the thread out through the nose by a Bellocqs sound and fix it to the cheek with plaster as suggested by Schlechtendahl (Münch. Med. Woch. Ap.30.1901) The withdrawal of the tube is greatly facilitated by leaving the silk attached as such skill is necessary in using the extractor supplied with Intubation instruments. When the tube is first introduced it sometimes gives rise to spasm of the parts in which case one should wait a few minutes till this relaxes and the tube slips into place. If after introduction no cough results, if cyanosis deepens and breathing ceases the tube should at once be withdrawn and the case tracheotomized.

DIFFICULTIES AND DANGERS ATTENDING INTUBATION

1. Cases are recorded where the exudate has been pushed further down into the trachea by the tube, causing suffocation and death. In such a case the prompt removal of the tube may result in forcible expulsion of the false membrane.

2. Asphixia may result from prolonged and futile attempts at Intubation.

3. Laceration of the tissues with production of false passages.

4. Cardiac syncope during the struggling.

The tube is generally removed about the 4th day and kept out if possible, if dyspnoea again supervenes re-introduction will be necessary. Northup (Art. on Diphtheria Nothnagel's Encyclop. of Prac. Med.) remarks that five days for a child over two years of age may be considered a fair average. At the Willard Parker Hospital the time allowed is four days and at the New York Foundling Hospital three days (loc,cit) Northup also believes the times has been shortened by the introduction of Antitoxin treatment,

In a paper by Biernacki and Muir (Brit,Med,Jour May14 1904) on Intubation for Laryngeal Diphtheria the tube was coughed up or removed for the first time

(a) In 9 cases within 24 hours, in these 7 did not require re-introduction.

(b) Of 7 cases on the 2nd day, 2 did not require re-intubation.

(c) Of 7 cases on the 3rd day 4 did not require re-insertion.

(d) Of 11 cases on the 4th day 10 did not require re-introduction.

(e) Of 9 on the 5th day 8 did not require re-insertion.

(f) Of 7 on the 6th day 5 did not require re-insertion

(g) One case on the 7th day did not require re-insertion.

Those authors are of opinion that the tube ought to be removed on the 4th day at the latest and left out if possible, that if by the 10th day the tube cannot be dispensed with Tracheotomy should be performed, of 7 of their cases when the tube was retained after the 9th day 5 came to tracheotomy the other two escaping re-introduction and tracheotomy.

The method of performing Extubation varies. It is perhaps better to leave the silk cord attached to the tube, but in case this has not been done or where the cord has been bitten through Park's method may be tied

The child is placed face downwards with the body slightly elevated, pressure is then made on the lower end of the tube through the anterior wall of the trachea (Park: Loomis. Thomson. Amer. Sys. Pract. Med.) Should this fail to extubate the extractor must be employed.

After removal of the tube close watch must be kept on the child in case any difficulty in breathing may arise. A small dose of Morphine 1/64 grain may be given subcutaneously, an ice-bag applied locally and a steam tent erected all with the intention of allaying irritation and swelling of the Larynx.

A few hours quiet rest after extubation will often tide a case over that period during which re-intubation is usually necessary, Prolonged cases of Intubation may give rise to great trouble and anxiety. The cause may be either persistence of the false membrane or some form of laryngeal stenosis consequent on the original disease or irritation caused by the tube leading to granulation tissue, cicatrices or abductor paralysis, Fortunately such cases are rare in occurrence but are none the less annoying when met with,

In all cases of Prolonged ~~Distribution~~ Intubation one would

select a vulcanite tube as calcareous deposits do not tend to form on those as on long-worn metal tubes. The most favourable cases of this class to treat are certainly those where false membrane is persistent as by the liberal use of Antitoxin this can generally be overcome, but the cause of prolonged retention in many cases appears to be a subglotic laryngitis with tendency to oedema. In cases due to abductor paralysis repeated intubation is necessary and ulceration is liable to ensue. In such also there seems to be a special proclivity to Broncho-pneumonia. Where Traumatism has led to ulcers and destruction of tissue with subsequent granulation and chronic stenosis, repeated intubation till the cicatricial tissue has lost its contractile power, offers perhaps the best hopes of recovery and much persistence is required but many such will even then come to Tracheotomy in the end and it must not be forgotten that difficulty will be encountered in getting rid of the tracheotomy cannula because of the stenosis in the larynx and also because the cannula after being worn (as is sometimes necessary) for months will itself no doubt have given rise to a certain

amount of stenosis in the region ~~and~~ of the Tracheotomy wound. This additional complication is more likely to ensue if in children injury has been done to the cricoid cartilage in performing the tracheotomy.

When the occlusion of the larynx or trachea is complete or nearly so owing to prolonged use of the intubation tube or Tracheal cannula the best results are likely to be gained by enlarging the tracheal wound (under general anaesthesia) and working from below rather than from above, a sound being passed upwards through the stenosed larynx. In this way less injury is likely to be done as in forcible attempts from above the laryngeal ventricles may be caught and damaged by the sound. If, by this means, one be successful in introducing even the smallest intubation tube much of the difficulty has been overcome and this should be worn continuously for a week or two, then intermittently therwafter till a cure is effected .

(This procedure was recommended by O'Dwyer in a paper read before the Brit. Med. Assoc. 1894). At the same time great care is exercised to keep the tracheal wound patulous because there is less

risk of extubation occurring during the act of coughing, ~~which~~ but should this accident happen, the child is not in such imminent danger of suffocation, as would be the case were the tracheal wound allowed to heal. To keep this wound patulous however is a difficult task, and some children will inevitably perish from one cause or another before the desired end is accomplished.

Considering the facts already discussed as to the comparative utility of intubation and tracheotomy one must conclude that the surroundings must be the main guide, certainly Tracheotomy in private practice. In hospital work with a skilled resident and nursing staff at hand, primary intubation unless otherwise contraindicated.

Gasparini (GazZ. degli.Osped.Feb. 18.1906) publishes observations on 150 cases of diphtheria. His mortality was 7.33% . He never gave more than 6000 units Antitoxin. Most of his remarks are, however, directed to a plea for intubation as against Tracheotomy. His experience of the latter operation was unfortunate, as out of the 3 cases tracheotomized all died — Gasparini regards

glottic spasm the main difficulty of intubation. The other complications he met with were haemorrhage, vomiting, and glottic oedema. Syncope never occurred in his hands. Bayeux' method of enucleation is recommended in cases of difficulty.
The thumb is placed at the point of the cannula in the crico-thyroid space the child's head being extended and then rapidly flexed. The usual time of wearing the tube was 3 to 5 days. This author although preferring intubation in hospital work, admits that in private practice Tracheotomy may be more advantageous on account of the constant after supervision of intubated cases.

Cuno (Munch. Med. Woch. May 14 1901) gives an analytical account of the treatment of diphtheria at Frankfort. Discussing the operations for Laryngeal obstruction he states that Tracheotomy is now only performed within the first few hours after admission into hospital. The mortality rate up to 1899 of Tracheotomy cases was not improved in proportion to non-operated cases -- The total mortality was 51 %.

In 1900 he substituted Intubation for Tracheotomy. In all he intubated 31 children with a mortality of

25.8 %. But in 21 out of the 31 cases he had to perform Tracheotomy later. Owing to the trouble he experienced from the local effect of long-continued wearing of the Intubation tube including the difficulty of extraction, stenosis of the larynx and upper trachea etc. led Cuno to modify the procedure. He intubates the child now when dyspnoea calls for operative treatment and a little later after mucus and membrane have been coughed up he chloroforms the child and performs Tracheotomy with the intubation tube in situ. By this means he gains the advantage of time for performing his tracheotomy and avoids the congested veins met with when respiration is impeded. He also finds the hard tube a good guide for entering the trachea of young children. Cuno reduced his mortality by this means to 23%, and considering this small reduction one cannot avoid thinking the "means to an end" are very severe and not likely to find favour with many observers as the advantages gained by Cuno's procedure are so small, haemorrhage is really not formidable even from congested veins and with care the trachea is not as a rule difficult to locate.

McCollom of Boston furnishes the following table

of cases treated during 1888-1903, which shows a reduction in death rate from 82.49% to 41.40% in laryngeal diphtheria treated by intubation since the introduction of antitoxin treatment. (Welch and Schamberg) Am. Contag. Diseases p.743)

PRE-ANTITOXIN PERIOD

Year	No of Incubation Cases	Deaths.	Mortality per cent.
1888	100.	78	78'00
1889	128	104	81'25
1890	93	79	84'94
1891	50	42	84'00
1892	65	56	86'15
1893	109	90	82'56
1894.	89	74	83'14
	634	523	82'49.

ANTITOXIN PERIOD

Year	No.of Incubation Cases	Deaths	Mortality per cent.
1895	118	64.	54'23
1896	224	145.	64'73
1897	146	67	45'88
1898	71	42	59'15
1899	192	63	32'81
1900	259	87	33'59
1901	184	58	31'52
1902	145	49	33'79
1903	139	37	26'61.
	1478	612	41'40

TREATMENT OF DIPHTHERITIC PARALYSIS

In the majority of cases of Diphtheritic palsies special treatment is unnecessary on account of their incomplete development and short duration. This applies specially to ocular and facial paralysis and also palaparesis where the voice merely is nasal, but if regurgitation occur, food should be slowly given and be of a thickish nature, if difficulty continue nasal feeding is indicated. Continued rest in all cases is essential. Rectal alimentation is safer to adopt if nasal feeding is impracticable on account of persistent struggling in a child, and especially if pharyngeal palsy be associated. When the voice is stronger and clearer, soft solids may be given again to test deglutition. When respiratory paralysis is present and mucus tends to accumulate in the pharynx larynx or Bronchi, the foot of the bed should be tilted up on blocks. Small doses of Belladonna may be given to diminish the amount of the secretion. General paresis requires rest, light nutritious diet and massage to the muscles along with electricity - applied by an interrupted current: Strychnine orally or by hypodermic injection should be given along with some preparation of Iron to combat anaemia, but vomiting must be carefully avoided, more especially

if there be signs of cardiac paresis, iron then is best avoided. In severe cardiac cases with vomiting strychnine is valuable and especially given hypodermically. Rectal injections of peptonized milk and Brandy every 4 hour should be resorted to. Early cardiac involvement, as already stated, is frequently fatal, so that the treatment is prophylactic. A strict enforcement of the recumbent posture is to be insisted on. Another drug of value in cardiac cases is adrenalin chloride. The dose to begin with being 5m of the solution. It should be gradually increased. Its great use as a cardiac stimulant is in the fact that children take it readily when they will often fight against alcohol and it is not toxic to the heart, it does not like brandy, give rise to vomiting. Adrenalin acts mainly by contracting the peripheral arterioles; when given for a rapid small and weak pulse an improvement soon becomes evident, the pulse becoming slower fuller and stronger. The general colour also improves. The cardiac syncopes which may occur during convalescence are amenable to hypodermic injections of brandy or strychnine, the patient being placed on the back and hot bottles applies to the extremities.

Comby(Clinique Infantile 1904 p.345) recommends renewal of antitoxin treatment for cases of Diphtheritic paralysis, but when given for relapses serum is apt to cause somewhat unpleasant and alarming results - rigors vomiting etc. and these symptoms, if induced in a severe case of cardiac or respiratory palsey, would be most undesirable and would do much to endanger the patient's life.

Recently prominence has been given to the value of formic acid in the treatment of muscular paresis and weakness and of its value as a tonic in convalescence from acute illness I can testify from personal experience The drug may profitably be given as Syrup of the Glyceroformates of Sodium and Potassium. (Duncan Flockhart & Co) the formula being:-

Sodii Format. gr ii

Potass. Format. gr ii

Syr. Glycero phos. Co. ℥i.

This dose I prescribe every 3 hours at first and later thrice daily. The improvement in muscular power and well-being is very marked: especially where muscle waste is much in evidence after feverish illnesses.

The action of the formates has been shown to be on the muscles themselves and the effects are more lasting than

that of Strychnine which acts on the muscles indirectly through the motor cells. Now in Diphtheria where paralysis is often due to peripheral causes the action of strychnine may be limited in cases where the nerve conduction is interrupted. In the formates where we get direct action on the wasted muscles we have therefore a powerful help in treating paralytic phenomena. Further, as the formates do not cause such a rise in blood pressure as does strychnine and adrenalin chloride, they become of immense value in the Cardiac complications of diphtheria where the heart is sustained by their aid but at the same time is not met with increased blood pressure to impede its already enfeebled action brought about through myocardiac changes.

Croom (Edin. Med. Journal Oct. 1906 p.341) has shown by his observations on 100 cases of Diphtheria treated by strychnine and antitoxin as against 100 treated by Formic acid and antitoxin that the Incidence of paralysis fell from 8% to 3% in similar types of epidemics. The type of paralysis noted after formate treatment was a mild one. The effect of Formic Acid on the Cardiac complications was also striking: an irregular and rapid pulse re-acting very quickly to a hypodermic injection of Formate of Strychnine which had previously been treated without

benefit by a hypodermic of hydrochloride of strychnine. The results are due probably to a gradual stimulation of striped muscle all over the body with direct stimulation of the heart itself increasing the restive power of the individual (Loc.cit. p.345). Croom also makes mention of the great reduction in the percentage of albumen in his cases namely from 30% to 10%. Clement and Huchard also record the diuretic action of Formates, and their influence in diminishing albuminuria in renal sclerosis. Here again the action of the Formates on diphtheritic albumina is not due to any direct action on the kidney but to an increased resistive power offered by the individual to the action of the Toxines.

SECTION V

PREVENTION OF DIPHTHERIA.

This subject may be approached from the following headings:

1. Prophylactic Serum Treatment which has been already dealt with (pp)

2. Separation of the sick from the healthy including control of school attendance.

3. Disinfection of infected places and articles etc.

4. Careful boiling of milk during Epidemics.

5. Choice of suitable dwelling and surroundings

The isolation of the sick is best obtained by removal to an Infectious Hospital - A separate pavillion for each infectious disease would, where attainable, be the most satisfactory way of minimizing the aerial risk which however as we have seen is comparatively small. As regards Home isolation the precautions already given under general treatment should be adopted and if possible 2000 cubic feet air space should be the minimum allowable for each patient. Control of Schools. Though with proper bacterial examination and control of suspects closure may not be indicated yet where such proper precautions are not available as is the case in

many towns and most country places closure of schools during Epidemics may have to be adopted. It may be objected that closure of the schools does not get away from the fact that the children may still play together in the streets and lanes and thus no advantage is gained. This argument is to some extent sound, but it must be observed that the conditions are really quite different. In the one the children are shut up in rooms, generally ill-ventilated and stuffy, and inhaling dust particles probably laden with the germs, while in the other they are in the open air and the danger of spread thus greatly reduced though not completely removed. Again the predisposing throat conditions are much more likely to be induced by the conditions existing in most schools than would be the case where the children are playing in the open air. Therefore in country districts at least the safest plan in the interests of the children's health would be, to close the school definitely for a time, to procure thorough disinfection of the buildings and where possible have the pupils clinically examined before re-assembling and where such examination was suspicious follow it up by a bacteriological examination. Dr Thomas (Brit. Med. Jour. Aug 27th 1904 p.431) has proved that much more careful examination

is required on the part of practitioners before sending back to school such cases as have been absent with throat affections. In many cases children are allowed to return to school with their throats teeming with Diphtheritic bacilli and where the medical attendant had certified them free from infection. The length of time which should elapse before a patient, who has had Diptheria may return to school depends on several circumstances. Two which stand out prominently are the Period of Incubation and the Question of Recrudescence of infectiveness. The Incubation period may generally be taken as from 2 -5 days. In some cases the infection seems to operate almost immediately on exposure to it and in others may be delayed as long as two weeks(Thorne). Should the infection reach an inflamed or abraded surface of the throat such as may result from Catarrhal sore throat, measles or scarlet fever, ~~and~~ there is no reason why the process of Diphtheria may not begin to operate at once. On the other hand the action may be delayed on account of an unsuitable soil such as a coating of mucus perhaps slightly acid in its reaction. Oertel (Ziemssen's Encyclop. Med:art, Diphtheria) says "The time which elapses between the moment when

when the diphtheria contagium comes into contact with the body and that when the development of the poison becomes subjectively and objectively appreciated, is variously stated. It depends on the Quantity and Quality of the infecting material itself, and on the power of resistence, as well as in the structure and texture of the tissues which permits the penetration and absorption of the diphtheritic matter with varying facility". Allowing for all those circumstances for preventive purposes 7 days practically covers the incubation period. There seems reason to believe that where the infection is conveyed by stored milk in which multiplication of the germs has occurred and also where the direct reception of the poison is into the stomach that the period of incubation is likely to be shortened.

RECRUDESCENCE OF INFECTIVENESS Astley Gresswell (Trans.Epidem.Soc. Lond.1885-86) gives evidence from quoted cases that under certain circumstances Diphtheria is apt to become a chronic malady and liable to recrudescence in such cases. Gresswell in prosecuting enquries into Diphtheria in different parts of the country finds that a considerable number of persons who have been affected with Diphtheria years ago have suffered almost

onstantly since with throat affections, their
hroats being pecularly sensitive to changes in
eather and liable to attacks of acute tonsillitis.
urther he adds that Diphtheria has occurred amongst
ersons associating with those who at the time have
een suffering from this condition. It has also
roduced evidence, which is not incnnsistent with the
elief that such conditions of the throat left after
n attack of diphtheria may be due to a continued
ojourn in them of the material of diphtheria and
hat the violent re-actions of the tonsils of those
ersons to weather changes involve the likelihood of
endering them diphtheritically infectious. After
iving a number of cases in favour of his theory
r. Creswell appeals to the analogy of glanders in
he horse which though it may to all appearances have
een cured yet manifests itself afresh months after
nd this independently of any renewed infection, also
o the anahogy of gleet in relation to Gonorrhoea.
It seems"he adds"to be justifiable to regard re-
rudescence of a disease, and which is apparently
eferable to the life of a parasite organism, as the
xpression of rejuvenescence of that organism" Assum-
ng that his theories are valid Gresswell believes
hat a person once infected with Diphtheria may remain
apable of transmitting infection for as long a period
s two years. Newsholme (Royal Med.Chir.Soc.June.24
904)

gives instances of infectivity continuing over 110 days. A case is recorded (Brit.Med.Jour.Dec.31.04) which shows how readily bacilli may become buried in the crypts of the Tonsils without reaching the surface for the ordinary swab to touch and also that bacilli may lurk for a month in the throats of contacts. In this case a boy contact had been in Quarantine for a month. Before returning to school a swabbing was taken of a yellow spot on the Tonsils The bacterial report showed no diphtheria organisims but only staphalococci and strepto-cocci. Three days later as the spot was still visible a plug of inspirsated pus was removed by a pair of sterile forceps, dissolved in water, stained, and fixed. Diphtheria bacilli were easily found. This boy had no signs of Diphtheria.

Gabritschewsky (Zeit.F.Hyg.Bd.XXXVl p.45) gives a historical account of the knowledge that not only from cases of Diphtheria but also from apparently healthy individuals and convalescents, virulent Diphtheria bacilli may be obtained from the secretions of the nose and throat. He finds that virulent organisims may be present for months in the secretions with remarkable obstinacy and individuals in whom this state of affairs exsist must be a

dangerous source of infection to others.

Certain it is that an attack of Diphtheria confers but little lasting protection against another attack and as a matter of practice skilled examination of the throat and nose secretions should continue for at least a fortnight after either contact with infectionsccases or recovery from an actual attack of the disease before permission is given to return to school, and the rules already formulated (pp 104) may be taken as a practical guide on this matter each case being carefully judged by clinical and bacteriological evidence.

DISINFECTION OF INFECTED PLACES AND ARTICLES.

This requires to be very carefully carried out for the bacilli will live for very long periods on infected articles. Dried on silk threads Abel reports them to have lived 172 days and on a child's toy kept in the dark for 5 months (Park 20th. cent. Pract. Med. Vol 1 p 20.). In dried membrane they have been found to remain virulent for 20 weeks. (loc cit.)

The two best methods of room disinfection of the present time are Formaldehyde gas or sulphur dioxide. The former does not injuriously affect fabrics, metals, paintings, carpets etc, and is the more

efficacous and less harmful of the two.
Formaldehyde is sold as a 40% solution called Formalin. The windows doors and all crevices in the room should be carefully sealed up and the infected articles spread out with their surfaces fully exposed to the gas. Clothes, linen, and towels may conveniently be suspended from clothes lines strung across the room. About 10 ounces of Formalin should be used for every 1000 Cubic feet of air space. The Formalin may be used as Tabloids sublimated by heat, or the liquid evaporated in a generator or lamp; or used as a spray. If the latter be used three pints of an equal quantity of Formalin and water should be used for 1000 cub.feet of air space. The spray is even more penetrating than the gas. After gaseous disinfection the room should be kept closed and sealed for 24 hours after which it is aired and sunned.

If Sulphur Dioxide be used 5lbs may be burnt for 1000 cub. feet of air space. It has the advantage over Formalin in killing not only bacteria but animal life. Fleas, vermin, etc, as well. The room is prepared as before. Flowers of sulpher are placed in an iron pan set in a tub of water and ignited by hot coals. The room is again left closed for 24 hours. For bedding and clothing disinfection by high

pressure steam is most useful. Milk is rendered safe by careful boiling. Exposure of the Klebs Loeffler bacillus to 140 F for 5 minutes destroys its vitality. The boiling point of milk is 214-218 F. Klein has shown that in milk, multiplication of the organisims ceases after 4 days at a higher temperature than 98.6 F where-as in Agar and Broth they grow rapidly at this temperature. In Epidemics traced to milk those persons who only take it in tea or coffee are likely to enjoy complete immunity. In the choice a suitable surrounding and dwelling place attention should be given to secure a dry site, clean soil and avoid oscillation of subsoil water. Freedom from effluvia of sewers drains and decaying matter is also desirable. Free movement of fresh air and ample sunlight will do much to prevent occurrence oc epidemics. Dr Creswell (loc.cit.) found that the conditions under which the persons whom the"Diphtheria imparting sore throat" occurred were from living without exception in unwholesome, badly ventilated surroundings with drainage defects. Like the Tubercle Bacillus the patho-genicity of the Diphtheria Bacillus is rapidly modified by exposure to sunlight and contact with fresh air whereas if

air be excluded the diminution of Toxicity effected by light is slight. Herein may be the explanation of the prevalence of Diphtheria and ill defined throat mischief amongst people inhabiting damp shaded localities so situated as to prevent due exposure of the dwellings and of the soil to the combined action of sustained sunlight and movement of air.